4D-150 Wet AMD Development Day

September 18, 2024

Forward-Looking Statements

This Presentation contains forward looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Presentation, including statements regarding our clinical development plans, strategy, future operations, future financial position, prospects, plans, and objectives of management, are forward looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words. We may not actually achieve the plans, intentions, or expectations disclosed in these forward looking statements, and you should not place undue reliance on these forward looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward looking statements. In addition, the forward looking statements included in this Presentation represent our views as of the date of this Presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward looking statements in the future, we specifically disclaim any obligation to do so. These forward looking statements should not be relied upon as representing our views as of any date subsequent to the date of this Presentation.

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This Presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

This Presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities.

2024 4D-150 Wet AMD Development Day Agenda

1	**4DMT Overview & Key Takeaways** David Kirn, CEO	6	**Phase 3 4FRONT Program Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology
2	**Wet AMD & 4D-150 Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology	7	**4FRONT Discussion** *Moderator*: Dhaval Desai, CDO
3	**Phase 1/2 PRISM Overview** Robert Kim, CMO	8	**Preliminary Commercial Considerations** Christopher Simms, CCO
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4DMT

Boldly Innovating to Unlock the Full Potential of Genetic Medicines for Millions of Patients

Key 4D-150 Takeaways in Wet AMD

1. **Robust & Durable Clinical Activity:** Across all populations studied, including recently diagnosed patients

2. **Tolerability:** Well-tolerated with profile comparable to approved anti-VEGF agents

3. **4FRONT Phase 3 Design:** Maximizes probabilities of clinical, regulatory & commercial success

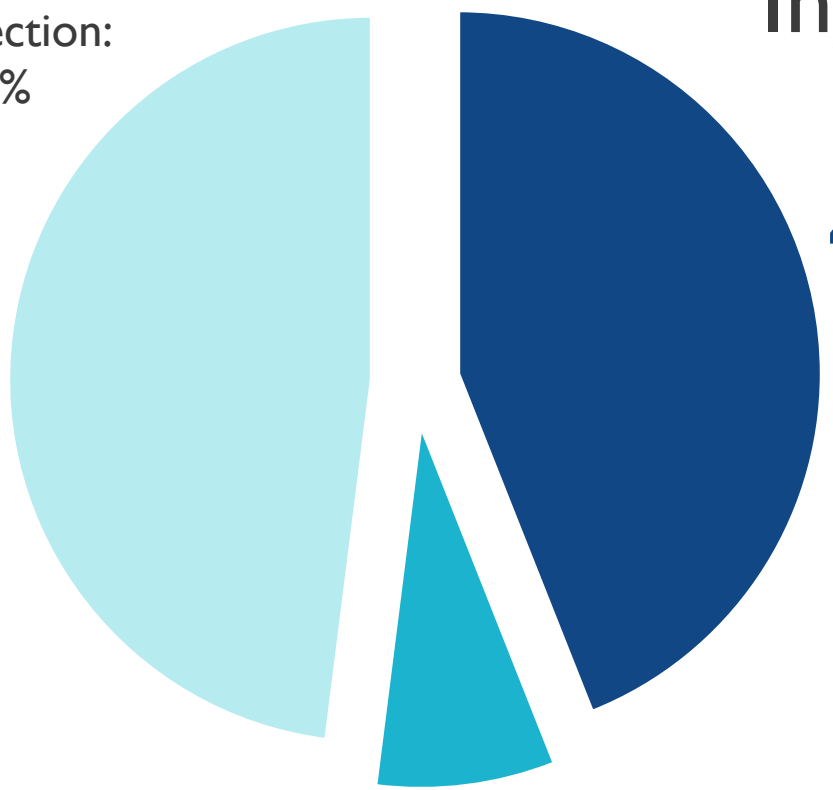
Data cutoff (clinical activity data), September 3, 2024.
Data cutoff (safety data), August 23, 2024.

Overview of Disease Populations

Cohort	Phase 1/2a (Dose Exploration & Expansion)	Phase 2b (Population Extension)	Phase 2b (Population Extension)
Population	Severe Disease Activity	Broad	Recently Diagnosed

In Severe Wet AMD Population

Through 52 Weeks†



Injection-Free:

44%

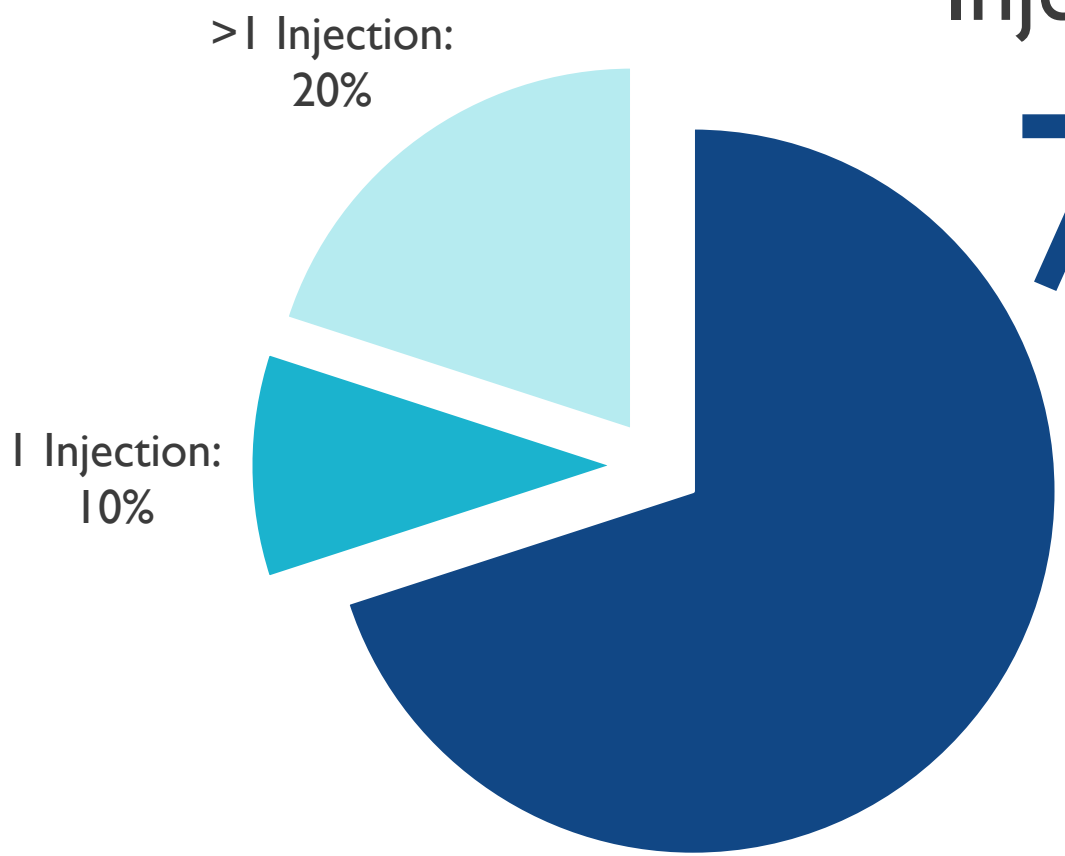
Treatment Burden Reduction:

83%

Data cutoff, September 3, 2024.
†Injection-free, 1 injection, and >1 injection based on Kaplan-Meier method for calculating endpoint with variable follow-up through 52 weeks (Phase 1/2a)

In Broad Wet AMD Population, Including Recently Diagnosed*

Through 52 Weeks†



Injection-Free:

70%

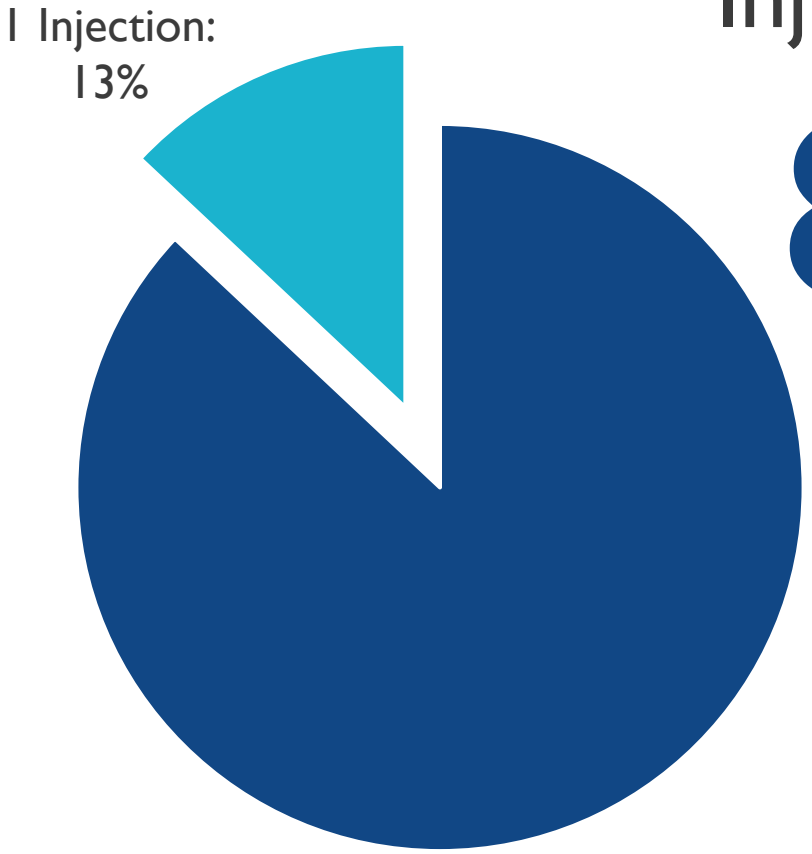
Treatment Burden Reduction:

89%

Data cutoff, September 3, 2024.
*Diagnosed ≤6 months prior to screening.
†Based on Kaplan-Meier method for calculating endpoint with variable follow-up through 32-52 weeks (Phase 2b)

In Recently Diagnosed Wet AMD Population*

Through 52 Weeks†



Injection-Free:

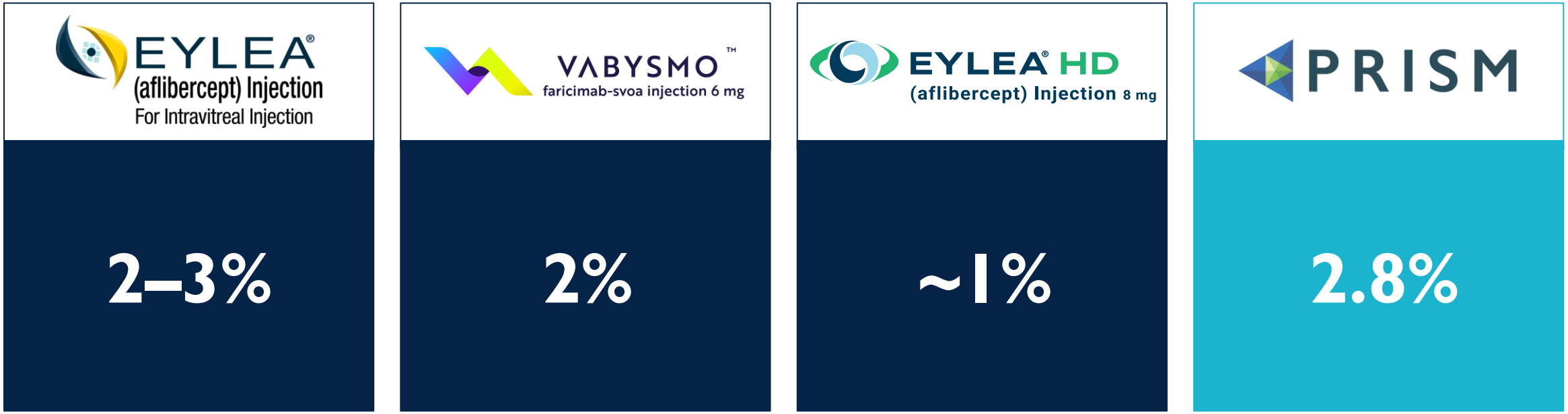
87%

Treatment Burden Reduction:

98%

Data cutoff, September 3, 2024.
*Diagnosed ≤6 months prior to screening.
†Based on Kaplan-Meier method for calculating endpoint with variable follow-up through 32-52 weeks (Phase 2b)

4D-150 Development Enabled by a Favorable IOI Profile



Data cutoff, August 23, 2024.
IOI, intraocular inflammation. All IOI rates from approved FDA labels.

4FRONT Phase 3 Program in Treatment Naïve Wet AMD Population

Design Maximizes Probabilities of Clinical, Regulatory & Commercial Success

1

Informed by:

- PRISM interim data
- Phase 3 designs of marketed intravitreal anti-VEGF products
- Regulatory discussions with FDA & EMA under RMAT & PRIME

2

Goals:

- Maximize probability of success for:
  - Primary endpoint: BCVA non-inferiority
  - Secondary endpoint: treatment burden reduction
  - Commercialization

3

Design features:

- Anti-VEGF responsive on study to be randomized
- 4D-150 3E10 vg/eye dose
- Durezol topical eyedrops
- 3 monthly loading doses applied to both arms
- Comparator arm 2Q8W dosing without supplemental injections

World Class Ophthalmology Advisory Board

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Chair

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Leader in retina gene therapy clinical research

Widely published and recognized International speaker

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Renowned speaker and author in retina

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Recipient of numerous prestigious awards

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President of EURETINA and Israeli Ophthalmology Society

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Editor-in-Chief of *Case Reports in Ophthalmology*

Dante Pieramici, MD

Investigator for 100+ trials

Co-developer of FDA-approved retinal drug delivery systems

Extensively published in retinal diseases

World Class Senior Ophthalmology Leadership Team:

100+ Years of Experience with Six Approvals & Five Launches of Major Products

Robert Kim, MD

Chief Medical Officer

30+ years

Clinical Science, Clinical Operations, Early- & Late-stage Clinical Development

Genentech — A Member of the Roche Group
NOVARTIS
Apellis
gsk
LUCENTIS RANIBIZUMAB INJECTION
SYFOVRE (pegcetacoplan injection)
Beovu (brolucizumab-dbll) Injection

Dhaval Desai, PharmD

Chief Development Officer

20+ years

Late-stage Product Development, Medical Affairs & Scientific Communications

IVERIC BIO An Astellas Company
NOVARTIS
izervay (avacincaptad pegol intravitreal solution) 2 mg
Beovu (brolucizumab-dbll) Injection

Christopher Simms

Chief Commercial Officer

25+ years

Pre-commercial & Commercial, Pre-launch Preparations & Development

IVERIC BIO An Astellas Company
NOVARTIS
Genentech — A Member of the Roche Group
izervay (avacincaptad pegol intravitreal solution) 2 mg
Beovu (brolucizumab-dbll) Injection
LUCENTIS RANIBIZUMAB INJECTION

Carlos Quezada-Ruiz, MD, FASRS

SVP, Therapeutic Area Head, Ophthalmology

20+ years

Leads Ophthalmology R&D, Early- & Late-stage Clinical Development

Genentech — A Member of the Roche Group
Roche
VABYSMO faricimab-svoa injection 6 mg
susvimo ranibizumab injection 100 mg/mL For Ocular Implant
LUCENTIS RANIBIZUMAB INJECTION

Today's Presenters

David Kirn, MD
Co-Founder & CEO

Robert Kim, MD
Chief Medical Officer

Dhaval Desai, PharmD
Chief Development Officer

Christopher Simms
Chief Commercial Officer

Carlos Quezada-Ruiz, MD, FASRS
SVP, Ther. Area Head, Ophthalmology

Arshad Khanani, MD, MA, FASRS
Director of Clinical Research at Sierra Eye Associates

Carl D. Regillo, MD, FACS, FASRS
Wills Eye Hospital

Dante Pieramici, MD
California Retina Consultants

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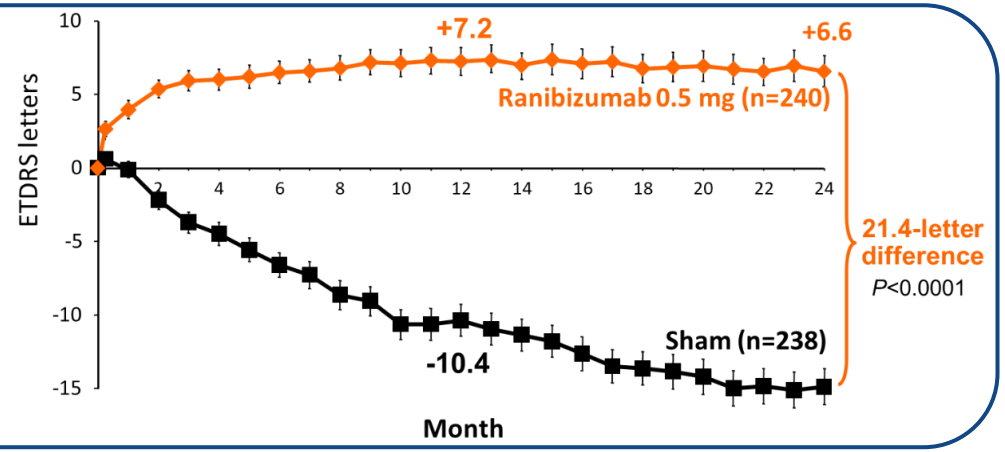
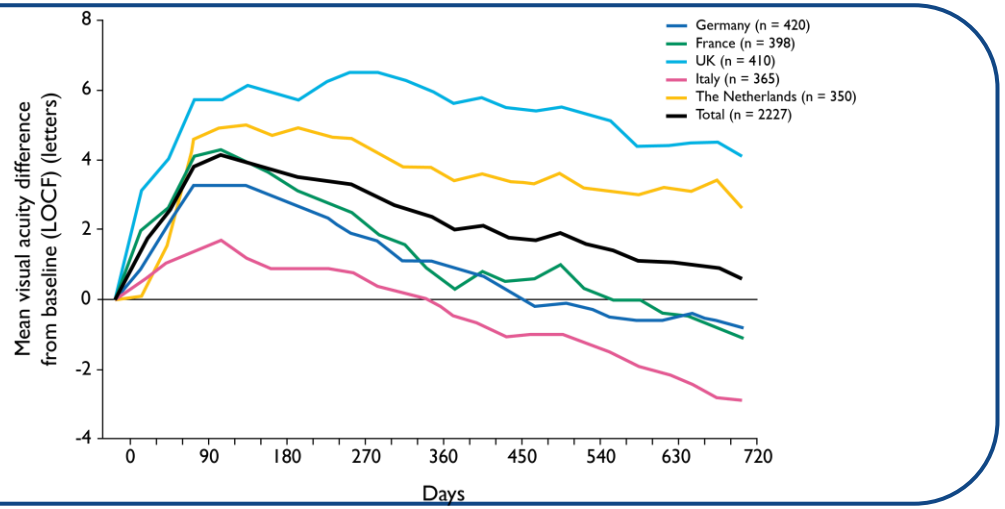
Retinal Vascular Diseases Are Still a Major Cause of Vision Impairment & Blindness[1] Despite the Introduction of Anti-VEGF Therapies >15 Years Ago[2]

- Wet AMD, diabetic macular edema, and diabetic retinopathy are among the **leading causes of moderate or severe vision impairment**
- Most patients in the real world **fail to achieve & maintain visual gains** seen in clinical trials
- **Major limitation of standard of care is durability**

MARINA: Frequent & Consistent Dosing Required to Maximize Vision Outcomes

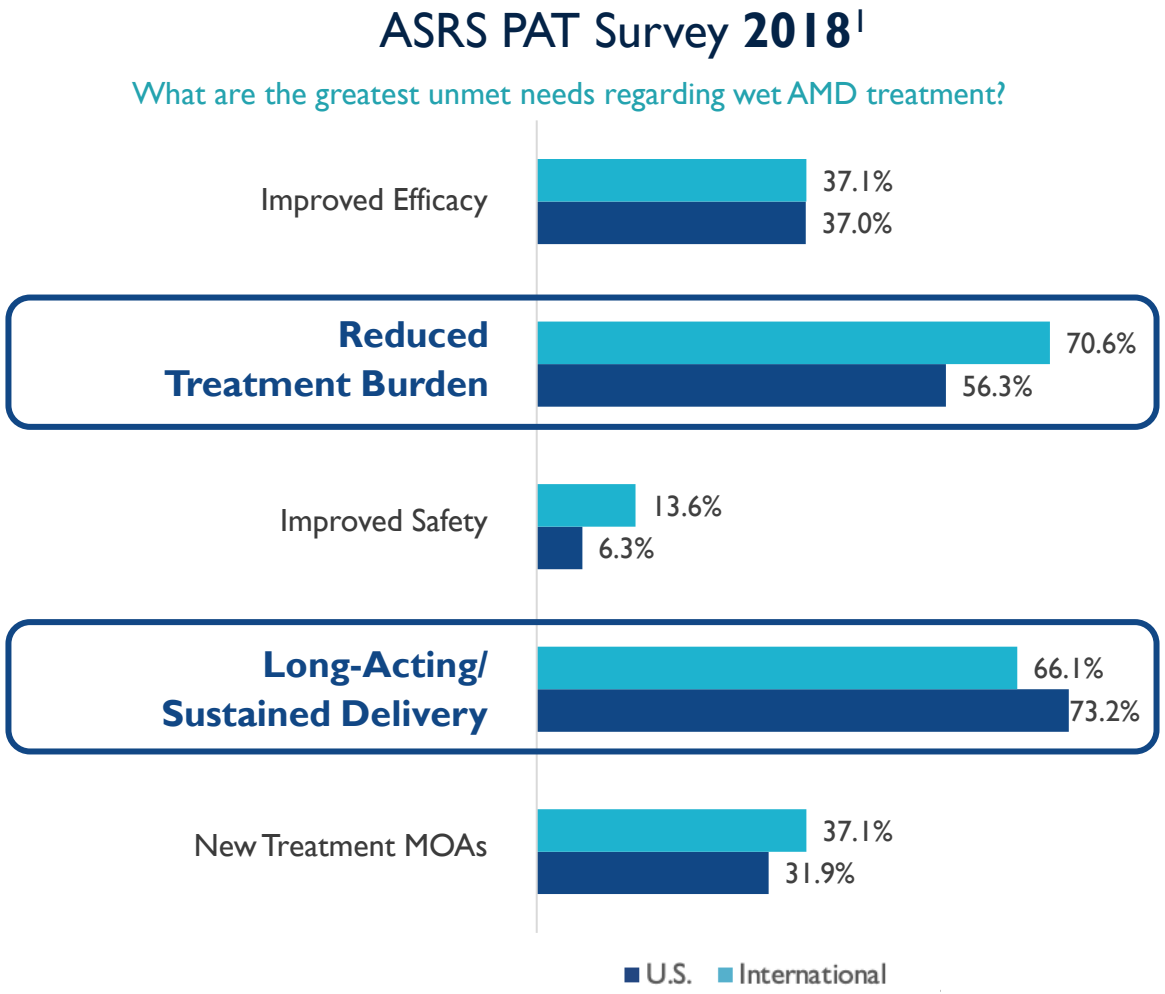


AURA[3]: Infrequent & Inconsistent Dosing in the Real World Results in Loss of Initial Vision Gains



1. Burton MJ, Ramke J, Marques AP, Bourne RR, Congdon N, Jones I, et al. The Lancet Global Health commission on Global Eye Health: vision beyond 2020. *Lancet Glob Health*. 2021; 9(4):e489–e551. 2. Rosenfeld PJ et al., *N Engl J Med* 2006;355:1419-31. 3. Holz FG et al. *Br J Ophthalmol* 2015;99:220-226

Largest Unmet Need in Wet AMD is Durable Efficacy with a Safe Treatment, Despite Recent Approvals of 2nd Generation Anti-VEGFs



1. Stone TW, ed. ASRS 2018 PAT Survey. PAT, Preferences and Trends.

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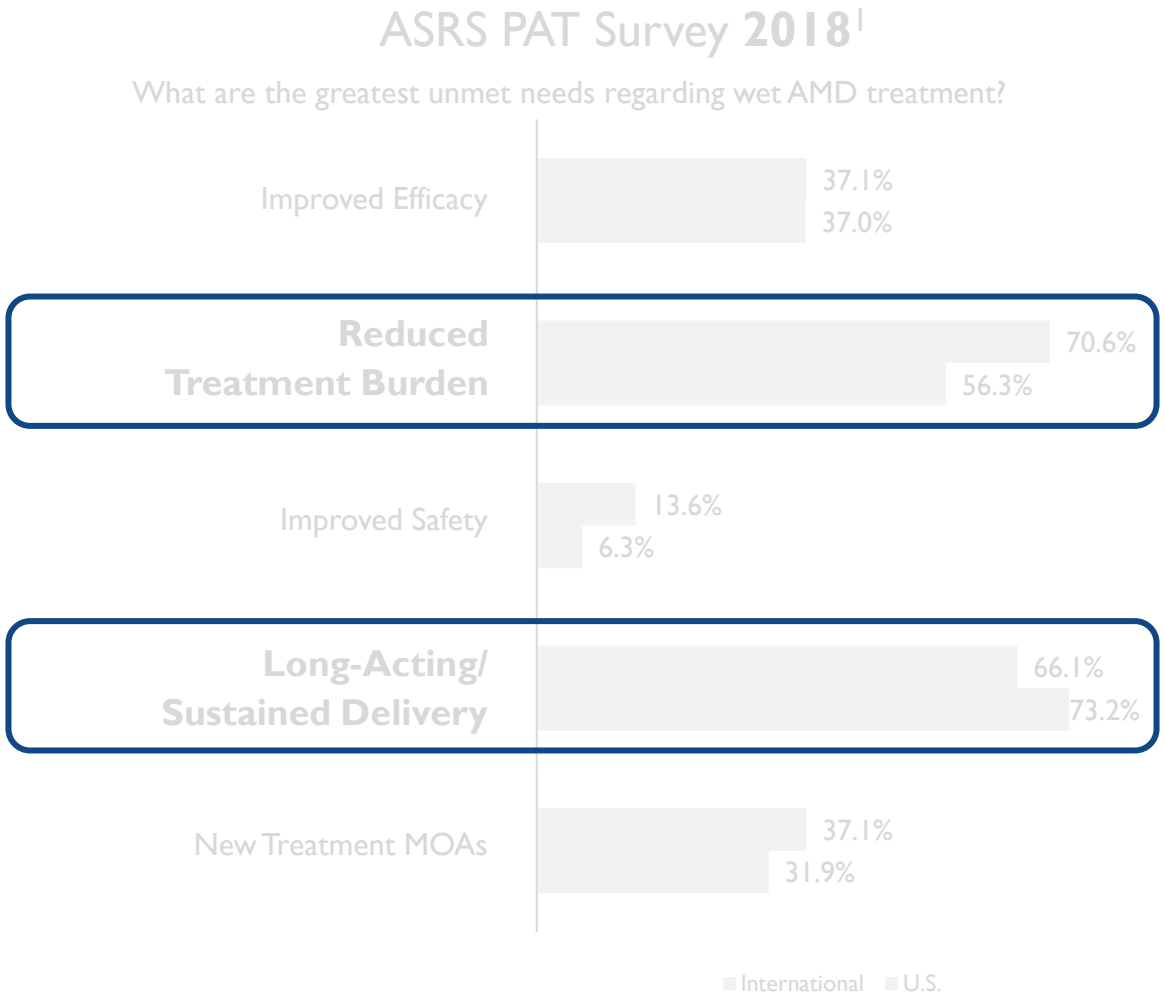

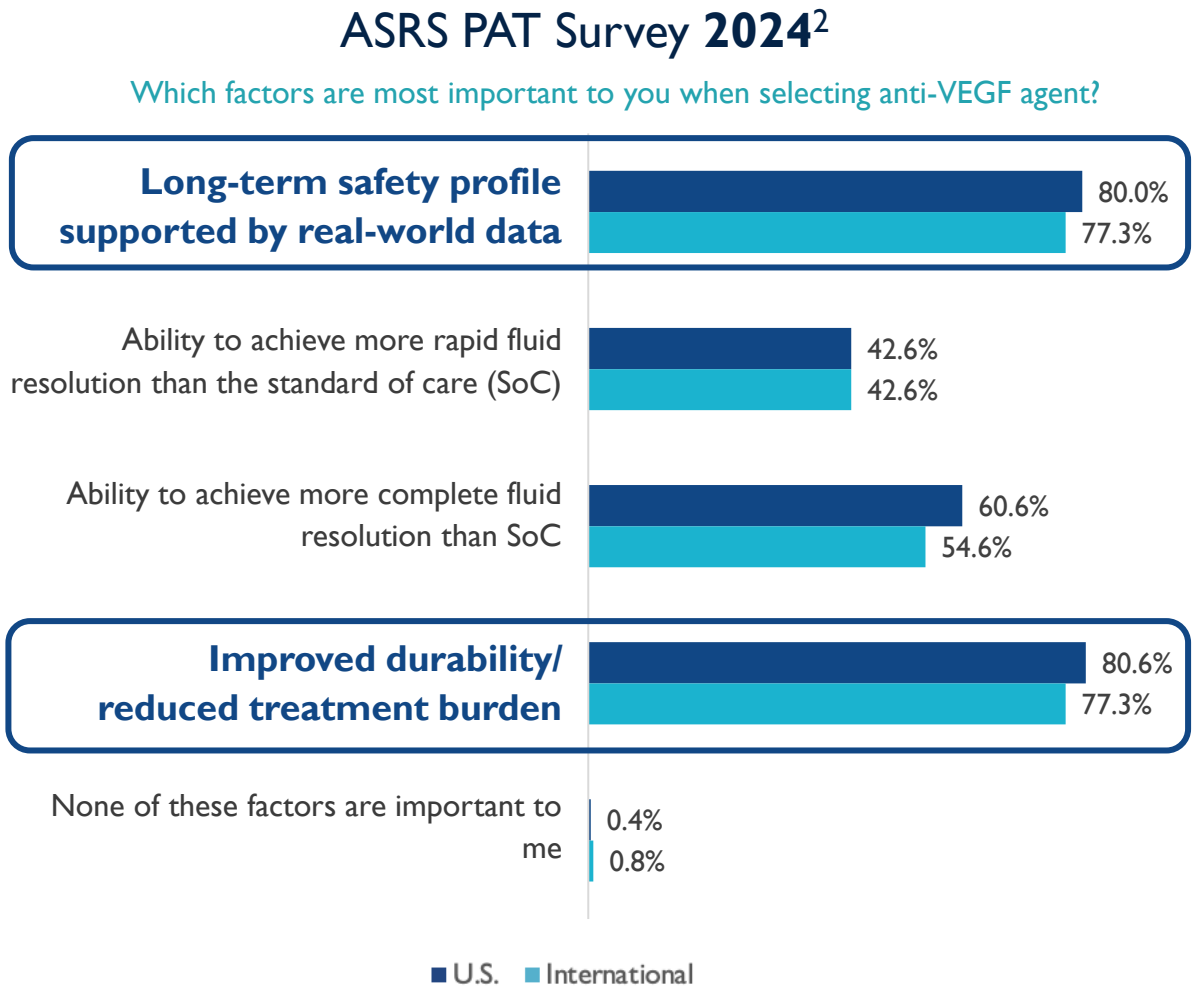

1. Stone TW, ed. ASRS 2018 PAT Survey. 2. Han P, ASRS 2024 PAT Survey. PAT, Preferences and Trends.

Ideal Therapy to Address Key Unmet Needs

Favorable Safety Profile

Comparable
to approved anti-VEGF agents

LUCENTIS® RANIBIZUMAB INJECTION

EYLEA® (aflibercept) Injection For Intravitreal Injection

EYLEA® HD (aflibercept) Injection 8 mg

VABYSMO™ faricimab-svoa injection 6 mg

Ideal Therapy to Address Key Unmet Needs

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Comparable
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2 Maximize Visual Outcomes with Extended Durability

Visual gains comparable
to approved anti-VEGF agents

Robust reduction of overall treatment burden

Long-term durability

Potential for
extended vision preservation

Ideal Therapy to Address Key Unmet Needs

1 Favorable Safety Profile

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2 Maximize Visual Outcomes with Extended Durability

Visual gains comparable
to approved anti-VEGF agents

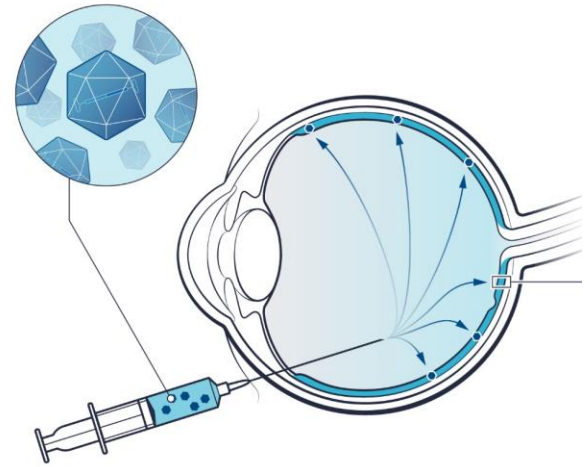
Robust reduction of overall treatment burden

Long-term durability

Potential for
extended vision preservation

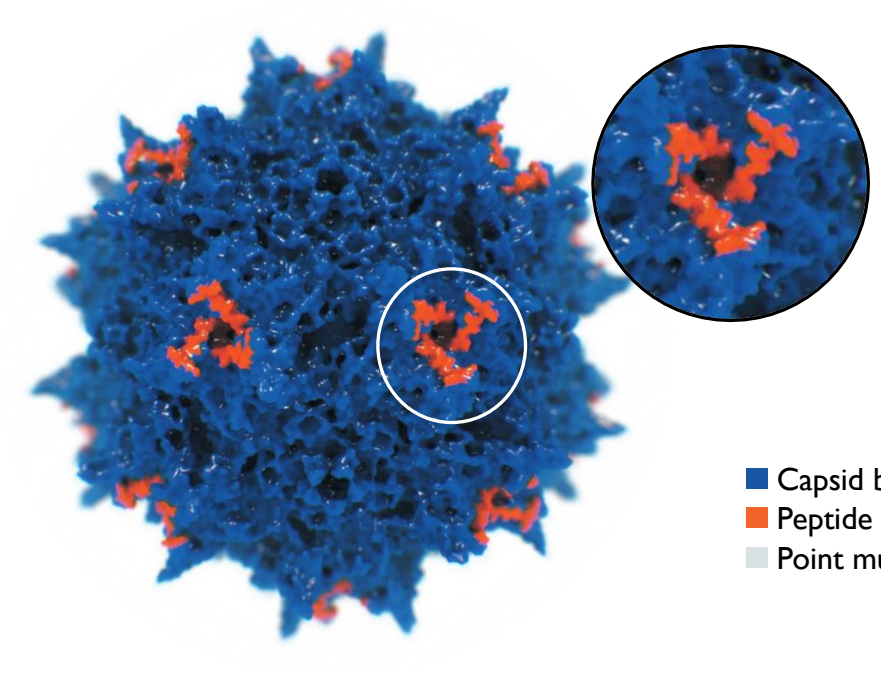
3 Route of Administration

Routine
intravitreal injection



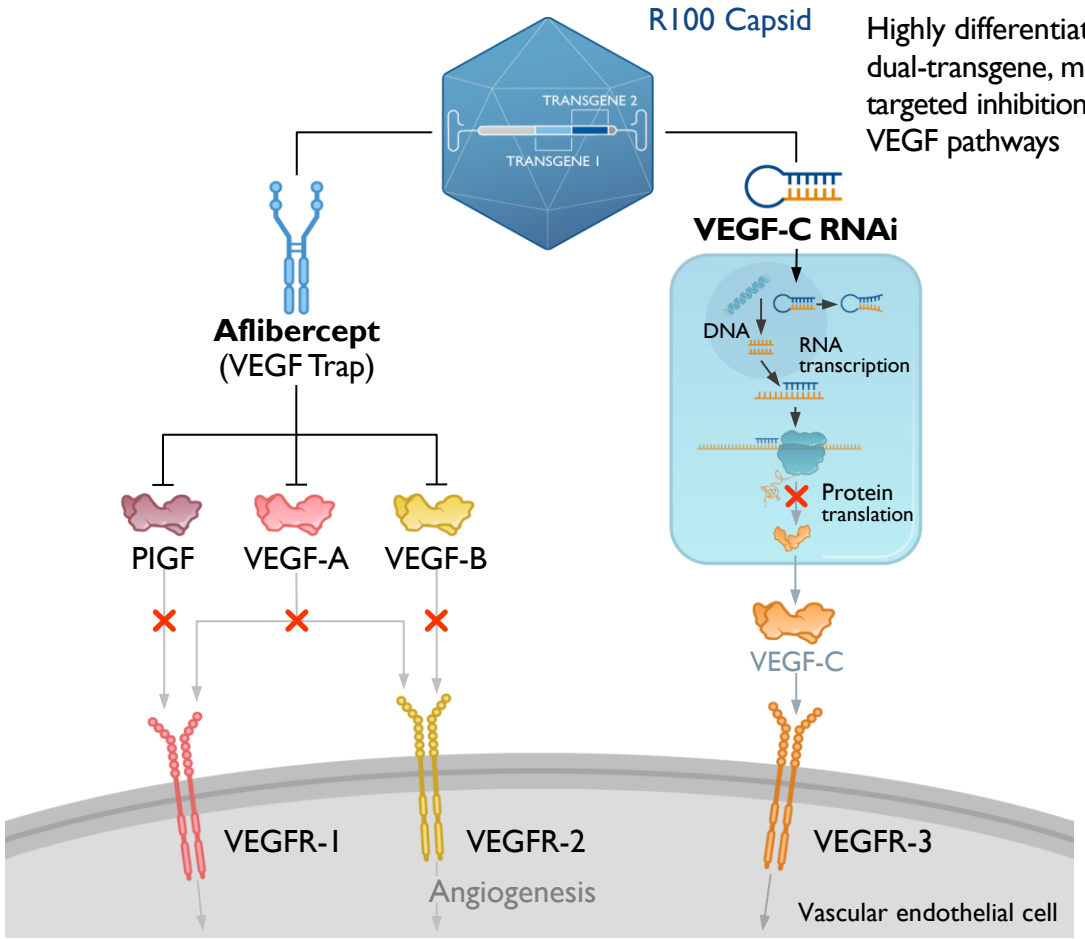
4D-150 Designed for Sustained Intraretinal Expression of Aflibercept & Blockade of VEGF-C Production to Address Key Unmet Needs

R100 Capsid



- ✓ Minimal inflammation potential based on clinical data to date
- ✓ Robust delivery to multiple retinal layers
- ✓ Durable expression of transgenes

4D-150



Abbreviations: ILM, inner limiting membrane; NHP, nonhuman primate; RPE, retinal pigment epithelium.

Rapidly Advancing 4D-150 into Major VEGF-Driven Retinal Indications While Building on the R100 Platform Beyond Anti-VEGF

VECTOR DELIVERY	PRODUCT CANDIDATE	INDICATION	EPIDEMIOLOGY (PREVALENCE)	PHASE 1	PHASE 2	PHASE 3
LARGE MARKET OPHTHALMOLOGY **R100** Intravitreal 	**4D-150** Aflibercept + VEGF-C RNAi	**Wet AMD**	*~3M U.S./EUMM*	4FRONT-1	4FRONT-1	4FRONT-1
				4FRONT-2	4FRONT-2	4FRONT-2
				PRISM	PRISM	PRISM
		Diabetic Macular Edema	*~5M U.S./EUMM*	SPECTRA	SPECTRA	
	4D-175 Short Form Complement Factor H	**Geographic Atrophy**	*~2.5M U.S./EUMM*	GAZE		

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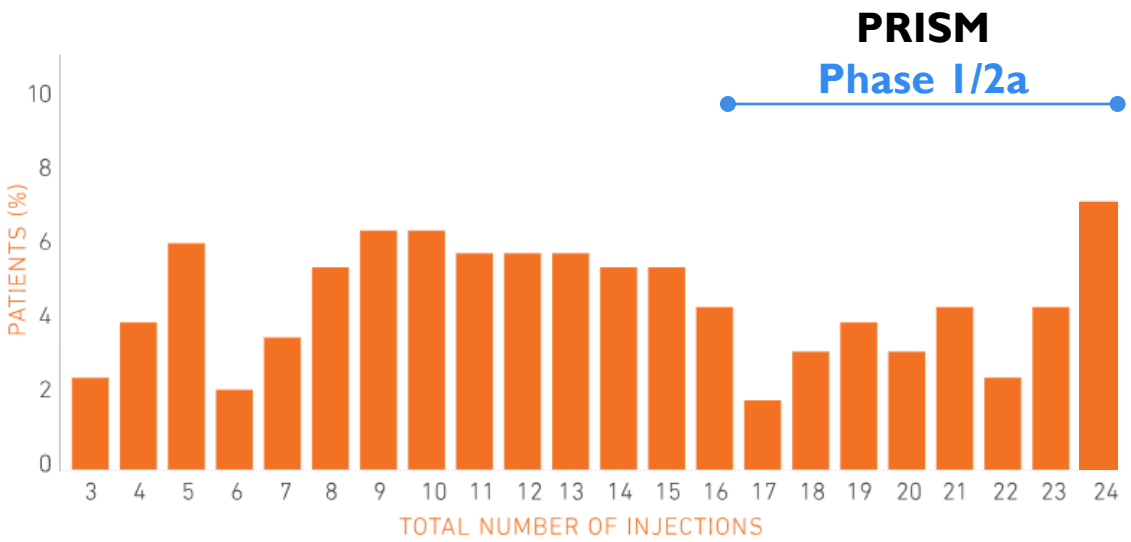
Anti-VEGF Treatment Need in Wet AMD Population is Heterogeneous: 4D-150 Development Moved From Highest Need Patients to a Broad Need Population

Lucentis HARBOR Study*



*Data on PRN ("as needed") injections received after 3 loading doses demonstrates a **high degree of heterogeneity in anti-VEGF needs in patients with wet AMD** (N=232)*

PRISM

- **Phase 1/2a: Severe Population**
  - Objectives: Safety, clinical POC
  - Enrolled: Highest anti-VEGF need & most severe disease activity population with long disease duration

*Lucentis.com

Anti-VEGF Treatment Need in Wet AMD Population is Heterogeneous: 4D-150 Development Moved From Highest Need Patients to a Broad Need Population

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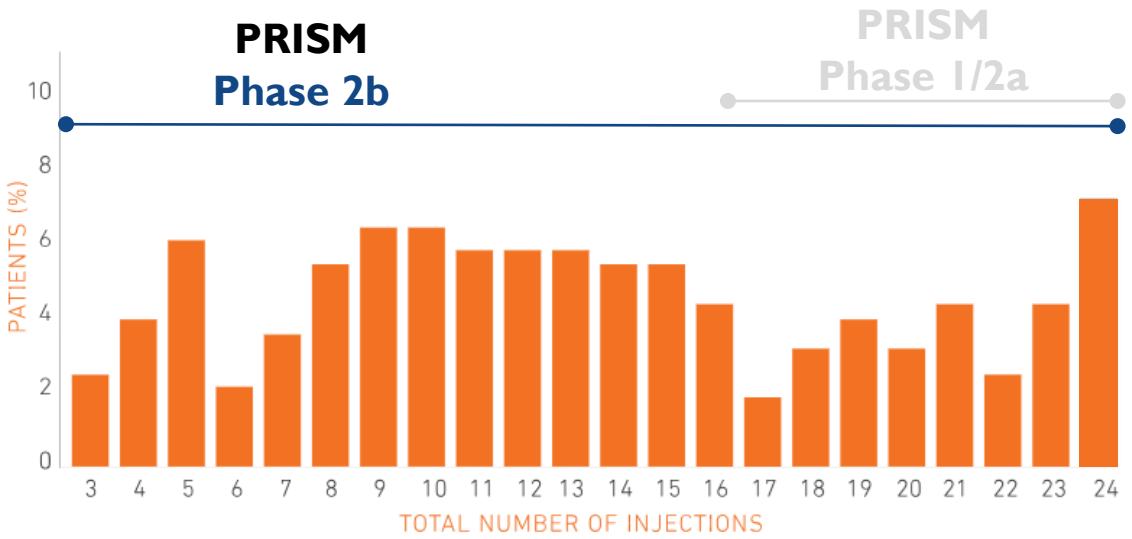


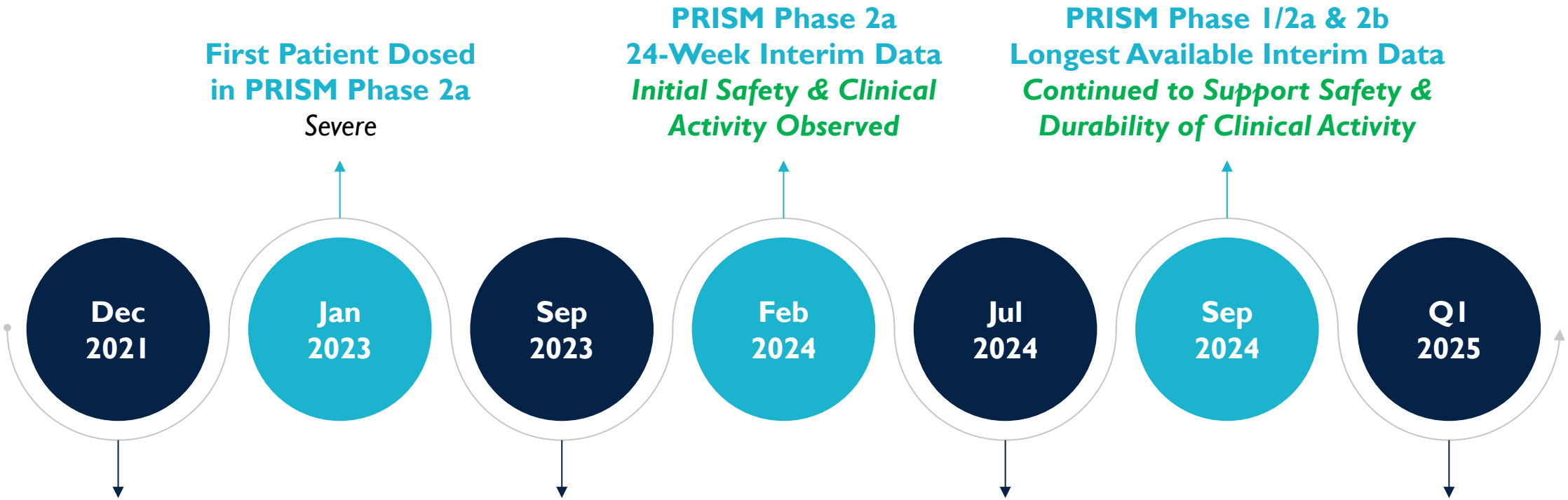
*Data on PRN ("as needed") injections received after 3 loading doses demonstrates a **high degree of heterogeneity in anti-VEGF needs in patients with wet AMD** (N=232)*

*Lucentis.com

PRISM

- **Phase 1/2a: Severe Population**
  - Objectives: Safety, clinical POC
  - Enrolled: Highest anti-VEGF need & most severe disease activity population with long disease duration
- **Phase 2b: Broad Population**
  - Objectives: Efficacy, Phase 3 dose & population
  - Enrolled: Broad range of patients with variable anti-VEGF need, disease severity & disease duration

4D-150 Development Program in Wet AMD: **First-in-Human to Phase 3 in ~3 Years**



*Patients diagnosed ≤6 months.

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Overview of Trial Populations Presented

Phase 1/2a: Severe

Dose Exploration & Expansion

Objectives:

To evaluate

- Safety
- Biological activity & clinical POC
- Doses for Phase 2b/3

Phase 2b: Broad

Population Extension

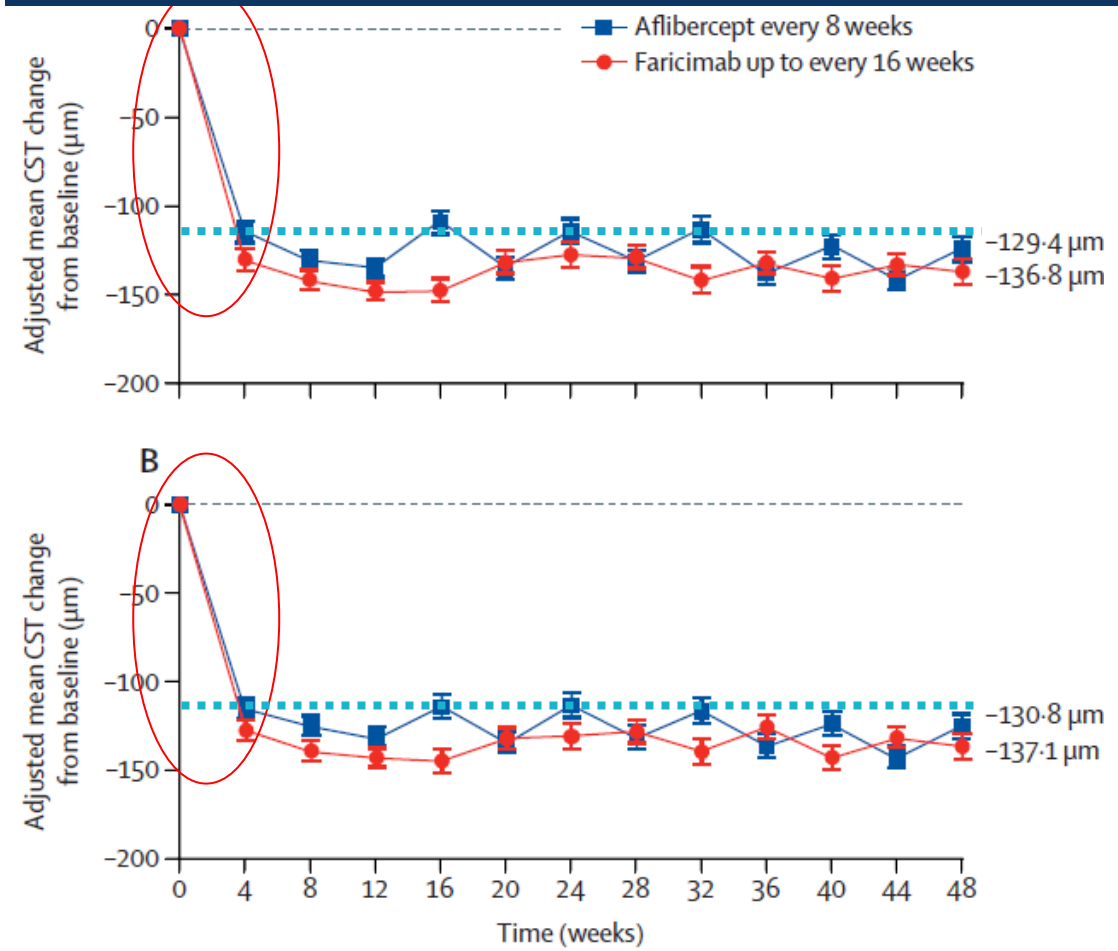
Objectives:

To determine

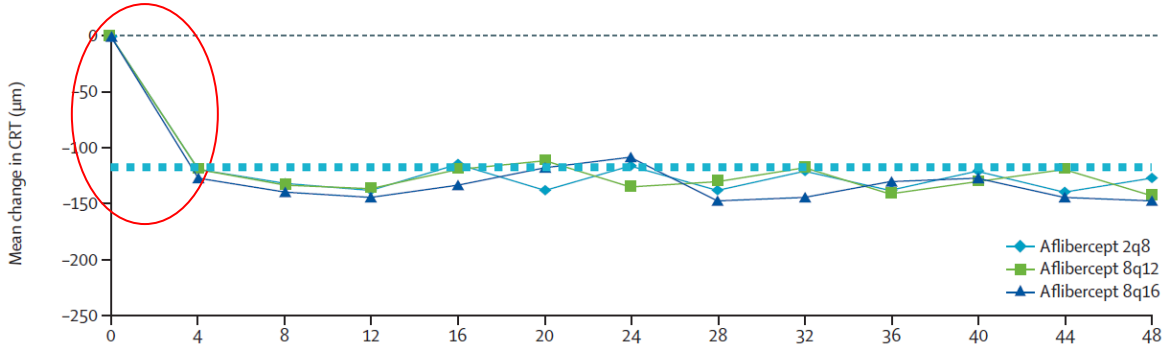
- Clinical activity in broad population, including recently diagnosed
- Selected Phase 3 dose
- Phase 3 patient population

Response to Anti-VEGF in **Treatment Naïve** Wet AMD: Majority of CST Benefit Observed with Initial Anti-VEGF Loading Dose

TENAYA / LUCERNE (VABYSMO)



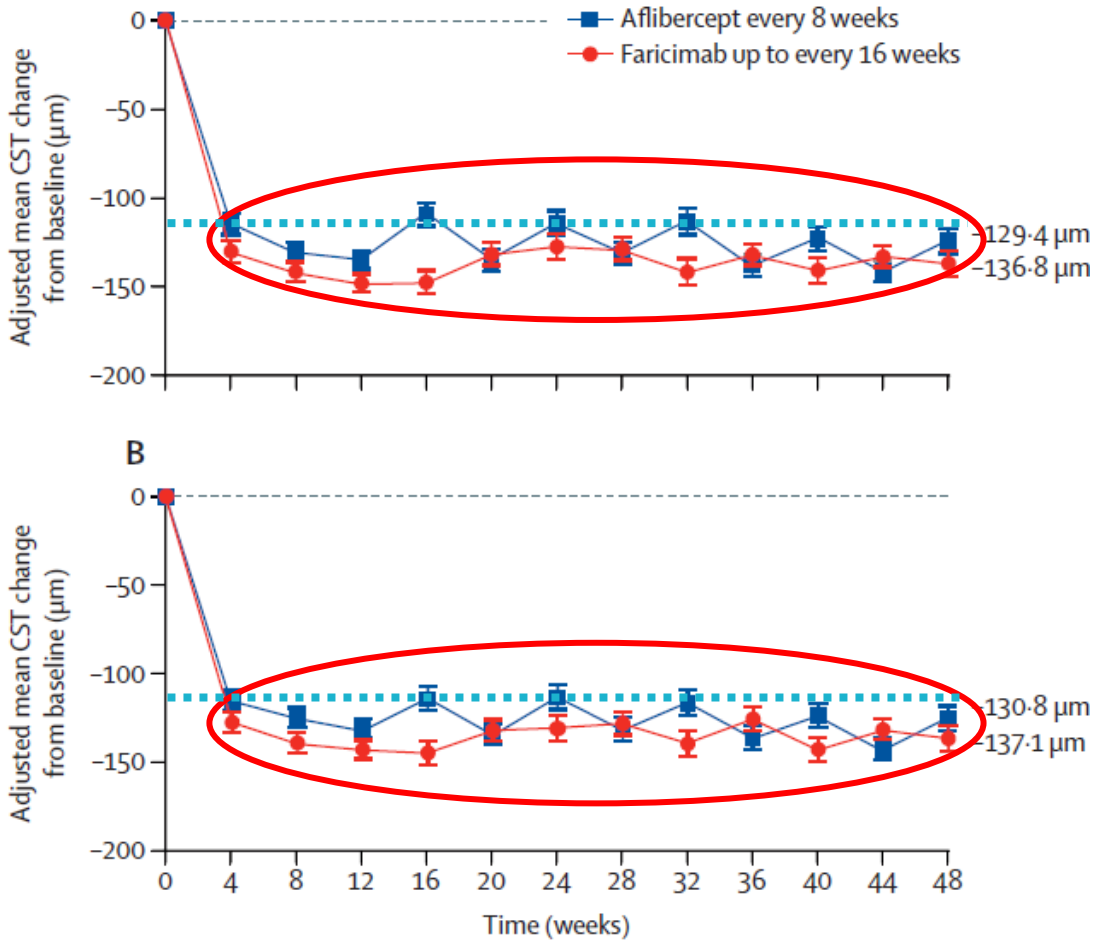
PULSAR (EYLEA HD)



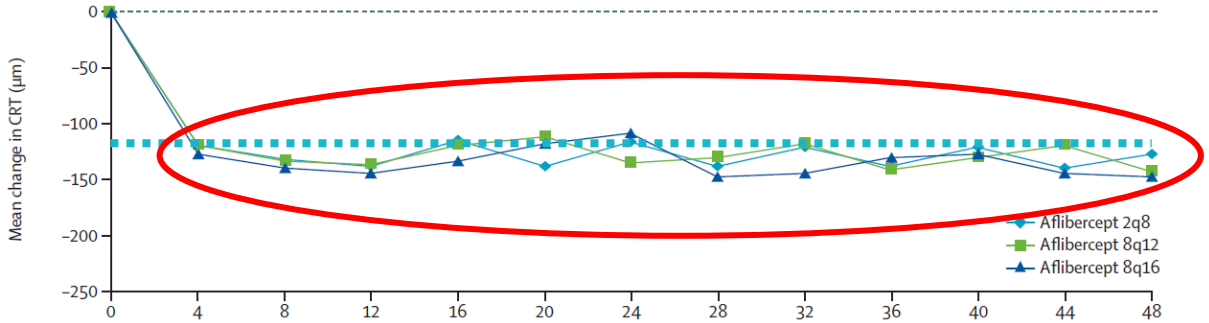
1. Khanani A et al. *Ophthalmol* 2024; 131(8): 914-26 (TENAYA & LUCERNE) 2. Lanzetta P et al. *Lancet* 2024; 403:1141–52 (PULSAR)

Response to Anti-VEGF in **Treatment Naïve** Wet AMD: Subsequent Injections Maintain CST Benefit Over Time

TENAYA / LUCERNE (VABYSMO)



PULSAR (EYLEA HD)

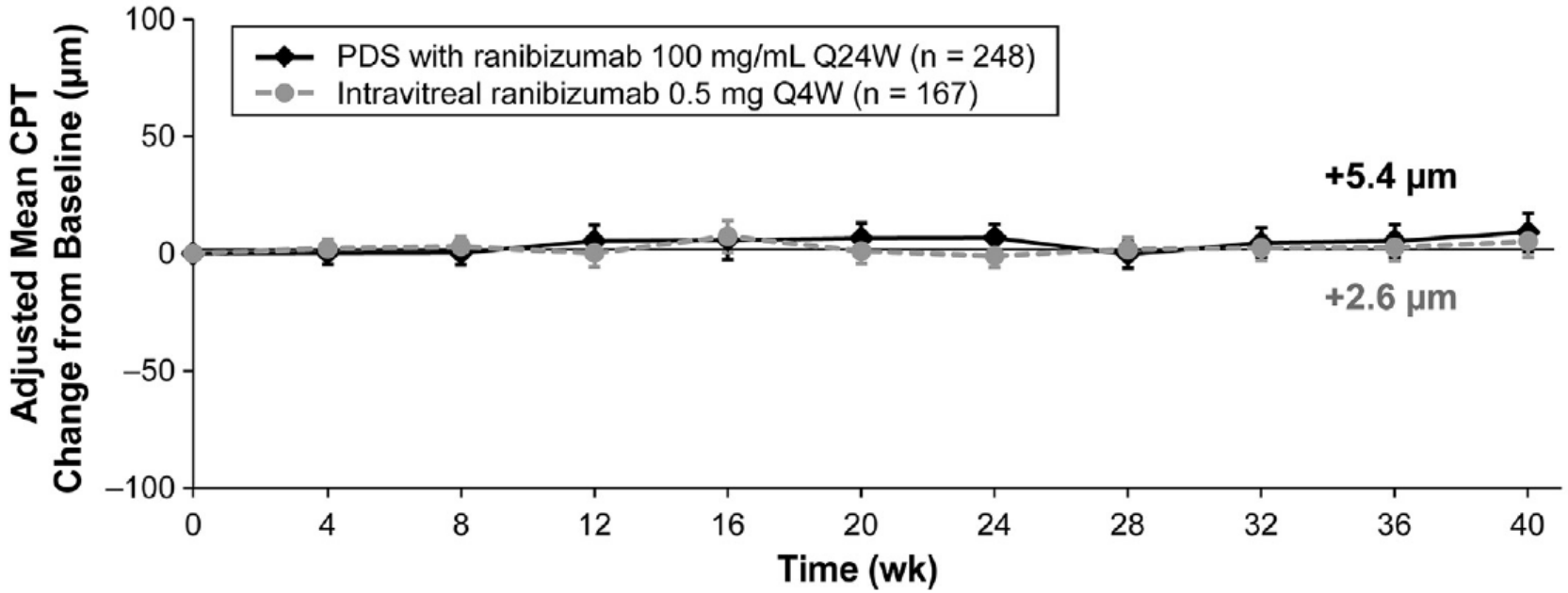


1. Khanani A et al. *Ophthalmol* 2024; 131(8): 914-26 (TENAYA & LUCERNE) 2. Lanzetta P et al. *Lancet* 2024; 403:1141–52 (PULSAR)

In Trials With **Previously Treated** Wet AMD Patients: Clinically Relevant Anatomic Outcome Measure is Maintenance of CST

ARCHWAY (SUSVIMO)

- Mean time since diagnosis: **5.6 months**
- Mean injections prior to enrollment: **5 injections**



"All Archway patients were treated previously with anti-VEGF injections to ensure responsiveness. As such, patients were likely at or approaching the plateau of possible vision gains or reductions in CPT in response to anti-VEGF treatment at the time of enrollment, leaving little opportunity for improvement from baseline in these parameters.[1]"

1. Holekamp NM et al. *Ophthalmol.* 2022; 129(3):295-307 (ARCHWAY)

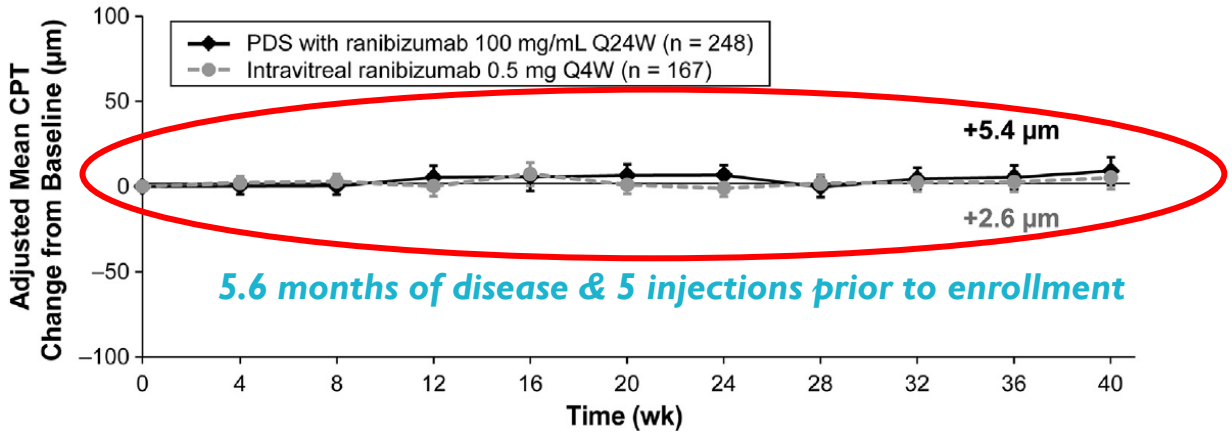
PRISM Population Compared to Recent Phase 3 IVT Wet AMD Studies

Asset	Study	Population	Mean time since Dx	Mean CST	Mean number of injections in previous year	Number of Loading Doses
EYLEA	VIEW1/2	**Treatment Naïve**	NA	313-342 µm	0	3
BEOVU	HAWK/HARRIER	**Treatment Naïve**	NA	360-370 µm	0	3
VABYSMO	TENAYA/LUCERNE	**Treatment Naïve**	67-74% within 1 month	350-360 µm	0	4
EYLEA HD	PULSAR	**Treatment Naïve**	NA	370 µm	0	3
SUSVIMO	Archway	**Previously Treated**	5.6 months	177 µm (CPT)	5	0*
4D-150 Ph1/2a (3E10)	**PRISM**	**Previously Treated**	**3.7 years**	**425 µm**	**10.2**	**1**
4D-150 Ph1/2a (AFLB)	**PRISM**	**Previously Treated**	**2.1 years**	**419 µm**	**9.3**	**1**
4D-150 Ph2b (3E10)	**PRISM**	**Previously Treated**	**1.8 years**	**336 µm**	**4.4**	**2**

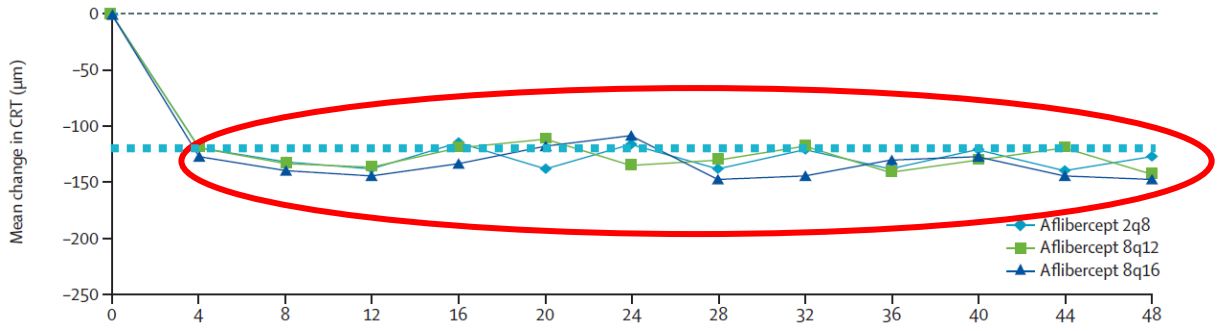
1. Heier JS et al. *Ophthalmol* 2012; 119(12):2537-48 (VIEW 1 & 2) 2. Dugel PU et al. *Ophthalmol* 2020; 127:72-84 (HAWK & HARRIER) 3. Khanani A et al. *Ophthalmol* 2024; 131(8):914-26 (TENAYA & LUCERNE) 4. Lanzetta P et al. *Lancet* 2024; 403:1141–52 (PULSAR) 5. Holekamp NM et al. *Ophthalmol* 2022; 129(3):295-307 (ARCHWAY)

Expected 4D-150 Response Based on Pretreatment Status and Historical Precedents

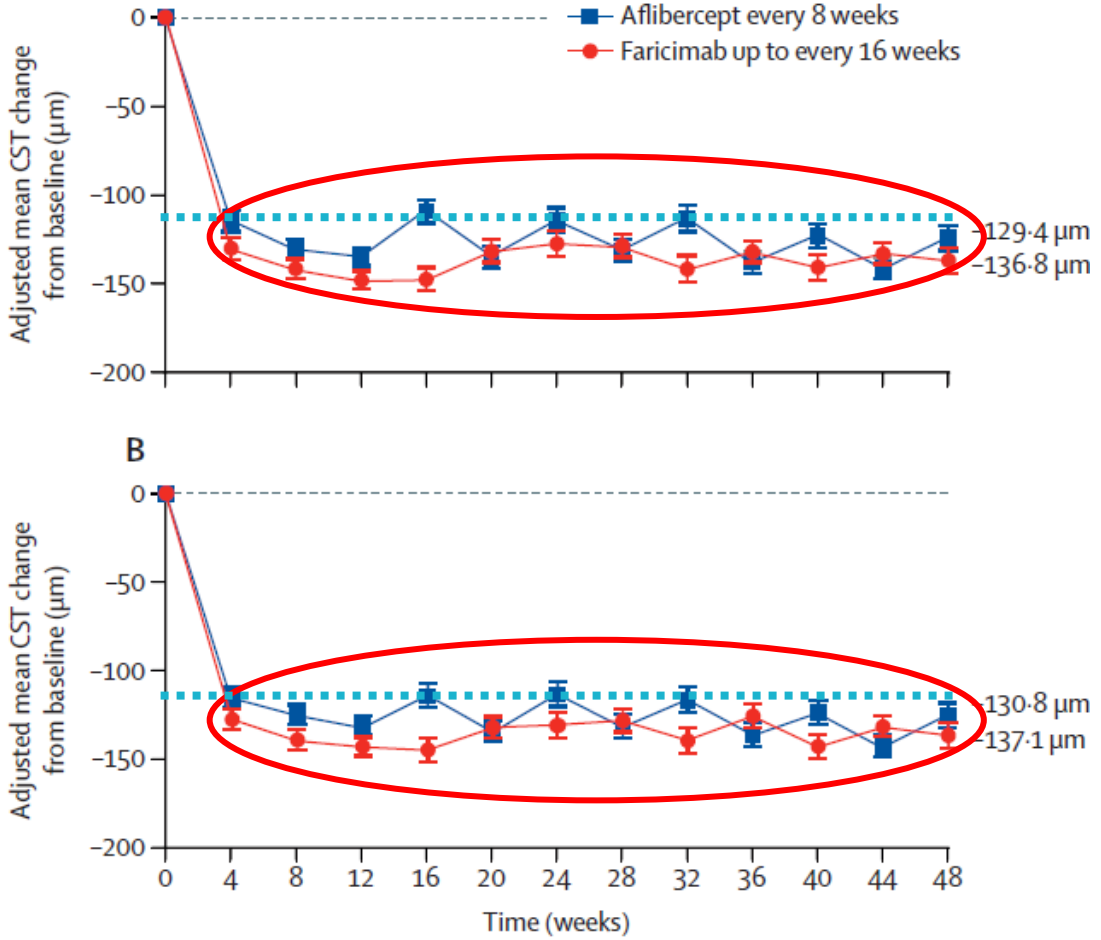
ARCHWAY (SUSVIMO)



PULSAR (EYLEA HD)



TENAYA / LUCERNE (VABYSMO)



1. Holekamp NM et al. *Ophthalmol* 2022; 129(3):295-307 (ARCHWAY); 2. Lanzetta P et al. *Lancet* 2024; 403:1141–52 (PULSAR); 3. Khanani A et al. *Ophthalmol* 2024; 131(8):914-26 (TENAYA & LUCERNE)

Phase 1/2a Interim Data

Follow-up: Through up to 130 weeks

4D-150 3E10 vg/eye & aflibercept control (N=34)

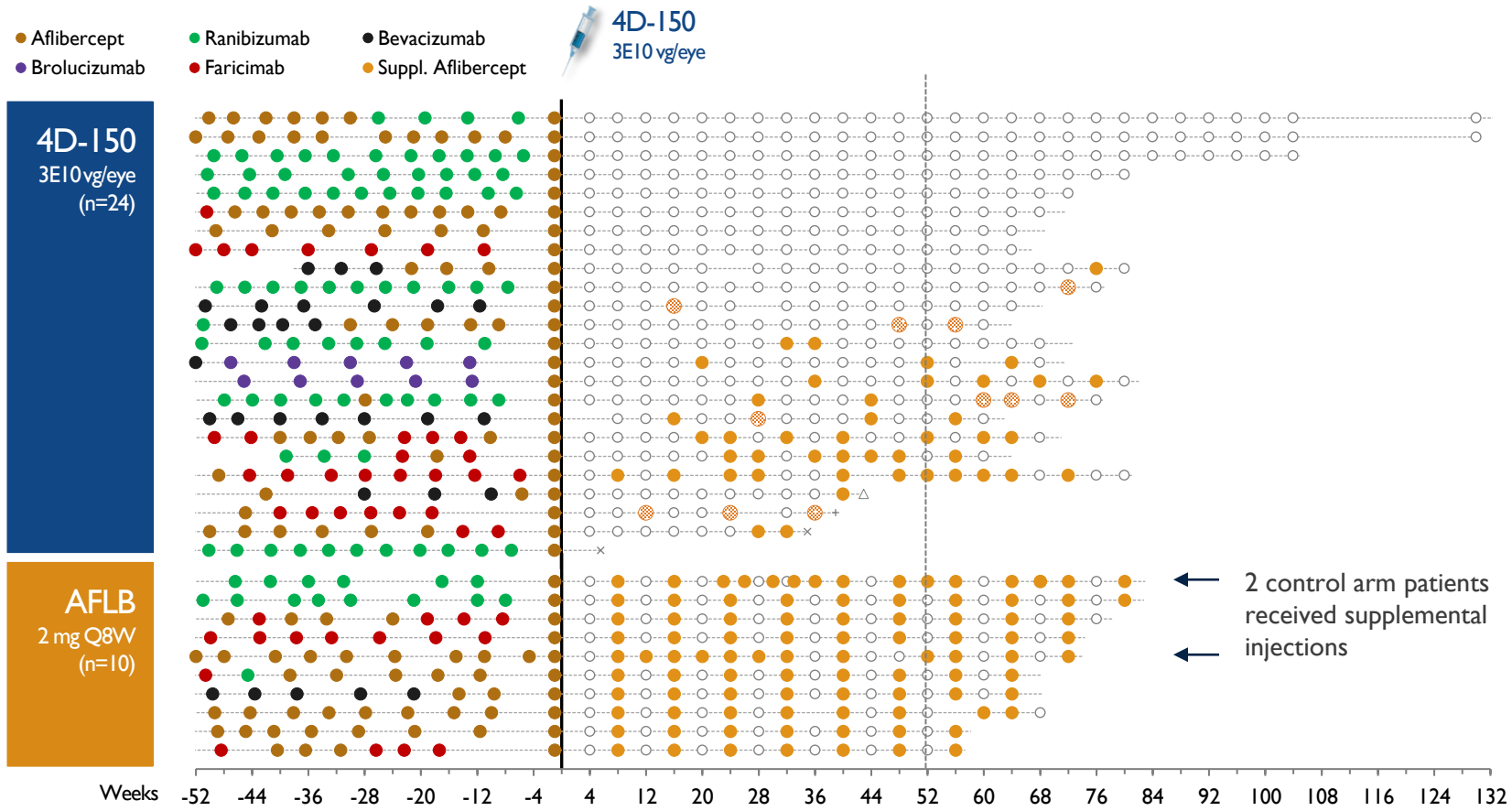
Data Cutoff Date, September 3, 2024

Efficacy Data Analyses:

Supplemental Injections

BCVA & CST

Phase 1/2a: >80% Reduction in Annualized Anti-VEGF Injections at Week 52 in Severe Disease Cohorts (3E10 vg/eye) with Strong Durability



Anti-VEGF Injections (Week 52)

Study Population	Annualized Reduction	Supplemental Injections*		
		0–2	0–1	0
Phase 1/2a (N=24)	**83%**	**73%**	**52%**	**44%**
Phase 1 (N=4)	**91%**	**75%**	75%	75%
Phase 2a (N=20)	**81%**	**73%**	47%	37%
AFLB Q8W (n=10)	28%	NA	NA	NA

*Kaplan-Meier estimates

Data cutoff, September 3, 2024.

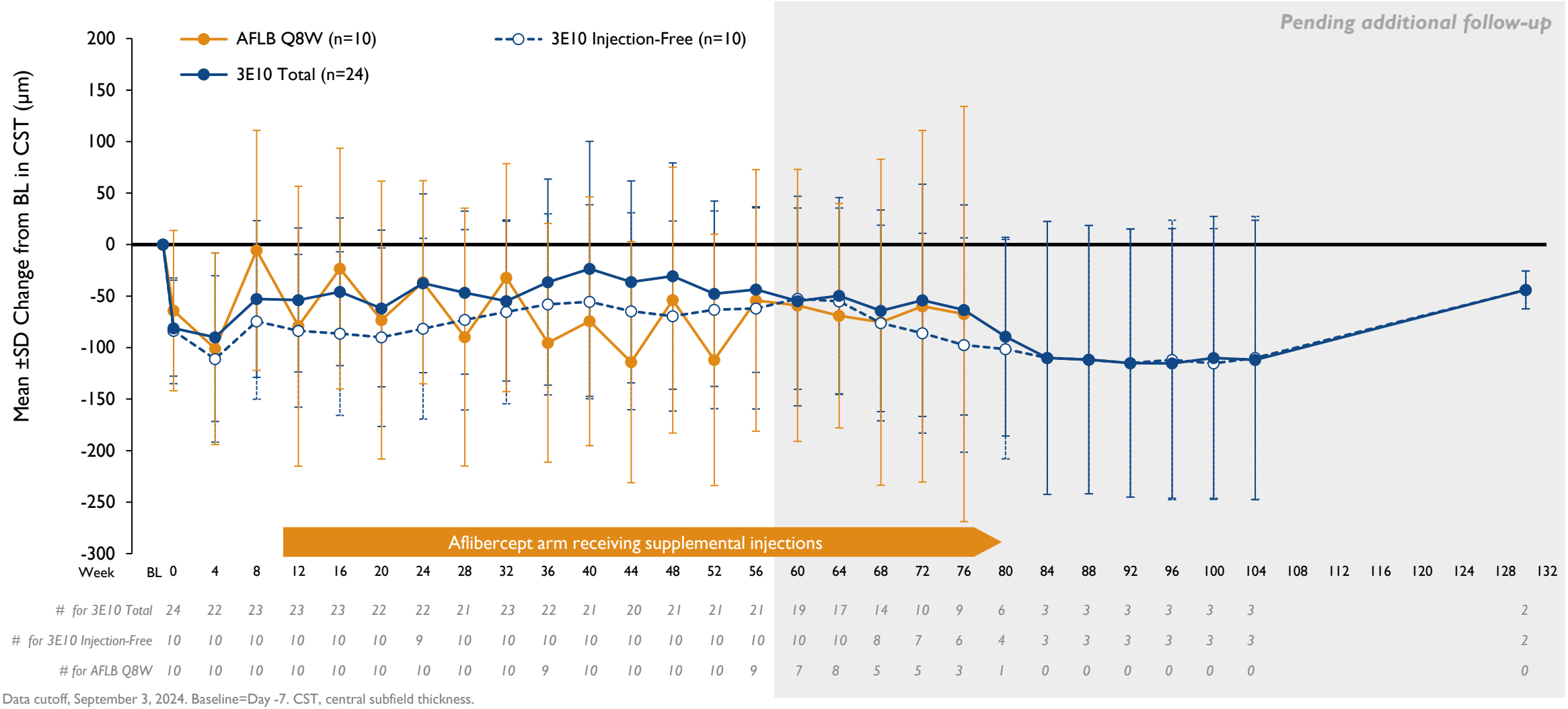
⊗ Supplemental injection administered based on investigator discretion (protocol-defined visual and anatomic criteria not met).

\+ Participant censored for supplemental injection assessment owing to protocol deviation (lost to follow up for >3 months after entering a nursing home).

× Early termination (death unrelated to study treatment), one of whom had missing data from Week 36 until death at Week 57.

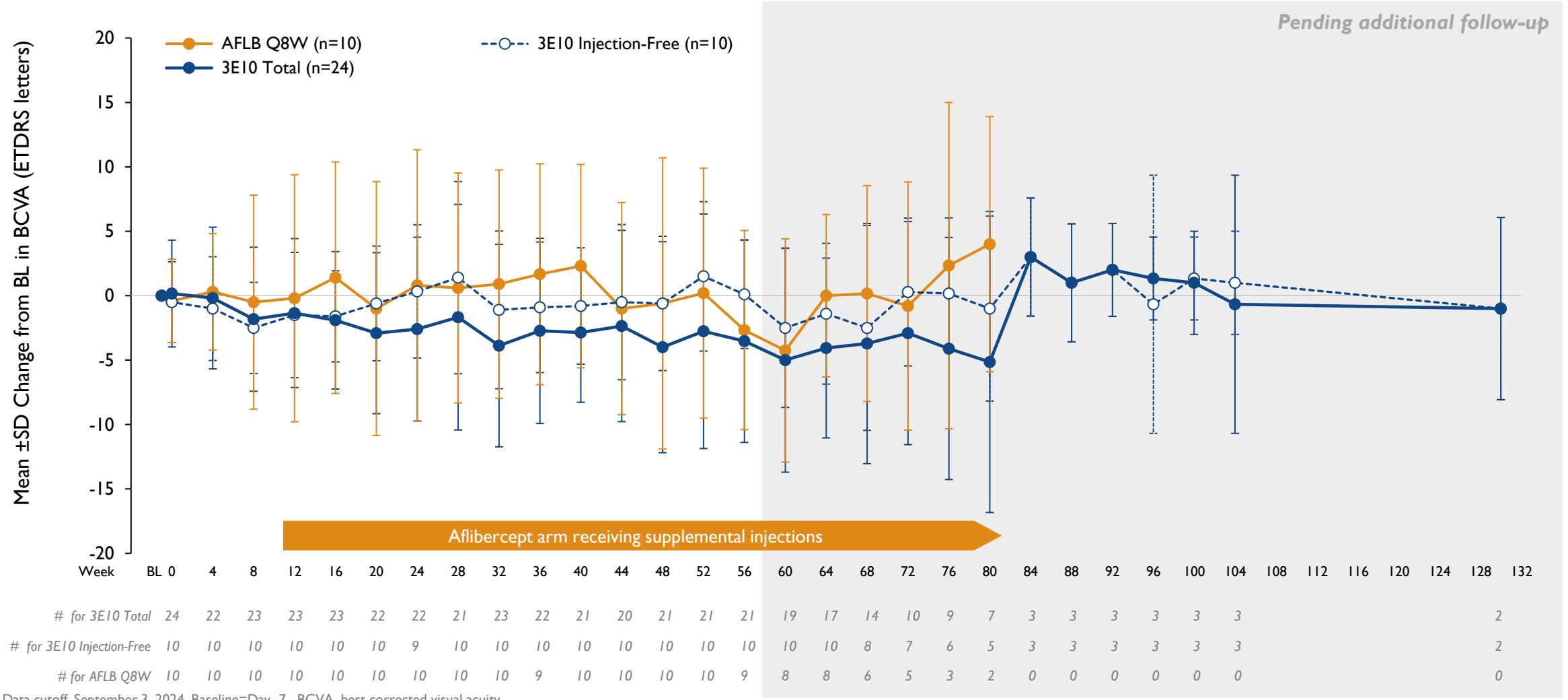
Δ Subretinal macular hemorrhage at Week 41; PI elected to administer 5 consecutive doses of aflibercept (4-week dosing interval) while blood resorbed (i.e., no new/ongoing hemorrhage); all 5 aflibercept injections were included in the calculation of mean annualized anti-VEGF injections. PI subsequently converted to an 8-week aflibercept dosing schedule; however, criteria for supplemental injection were not present. At week 104, the mean change from baseline in BCVA was -1 letter and the mean change in CST was -71 μm.

Phase 1/2a (4D-150 3E10 vg/eye): Sustained Anatomic Control With Fewer CST Fluctuations



Data cutoff, September 3, 2024. Baseline=Day -7. CST, central subfield thickness.

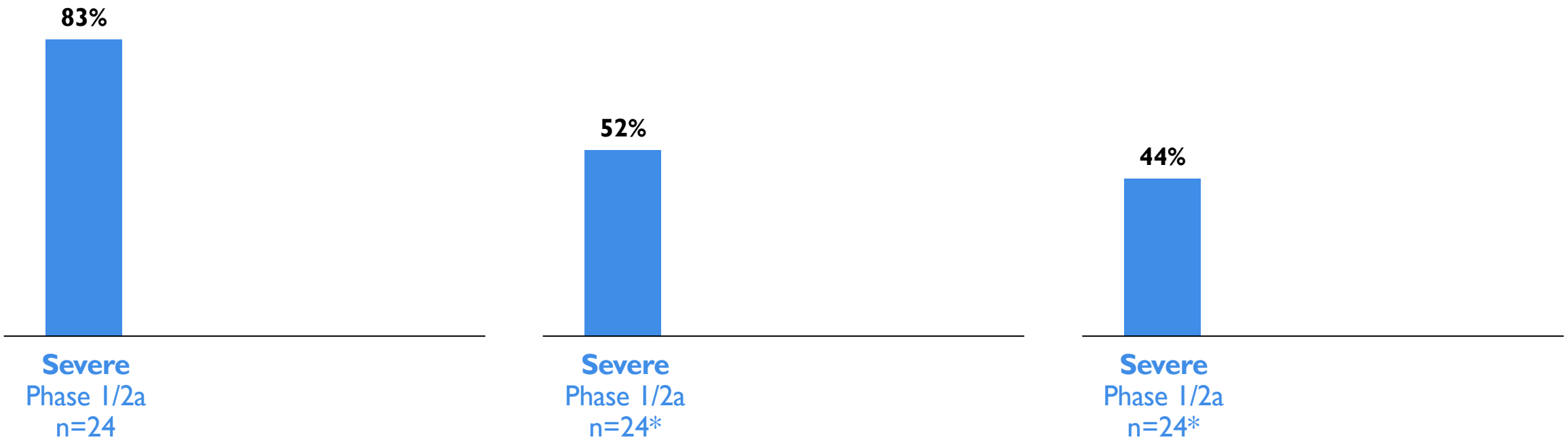
Phase 1/2a (4D-150 3E10 vg/eye): Visual Acuity Comparable to Aflibercept Q8 Week



Data cutoff, September 3, 2024. Baseline=Day -7. BCVA, best corrected visual acuity.

Robust & Durable Reduction in Treatment Burden in Severe Wet AMD Patients **Through 52 Weeks** (Phase 3 Dose: 3E10 vg/eye)

% Reduction in Annualized Injections	% 0–1 Supplemental Injections	% Supplemental Injection-free



Data cutoff, September 3, 2024.
*Based on Kaplan-Meier method for calculating endpoint with follow-up through 52 weeks (Phase 1/2a).

Phase 2b Interim Data

Follow-up: Through up to 52 weeks

4D-150 3E10 vg/eye (N=30)

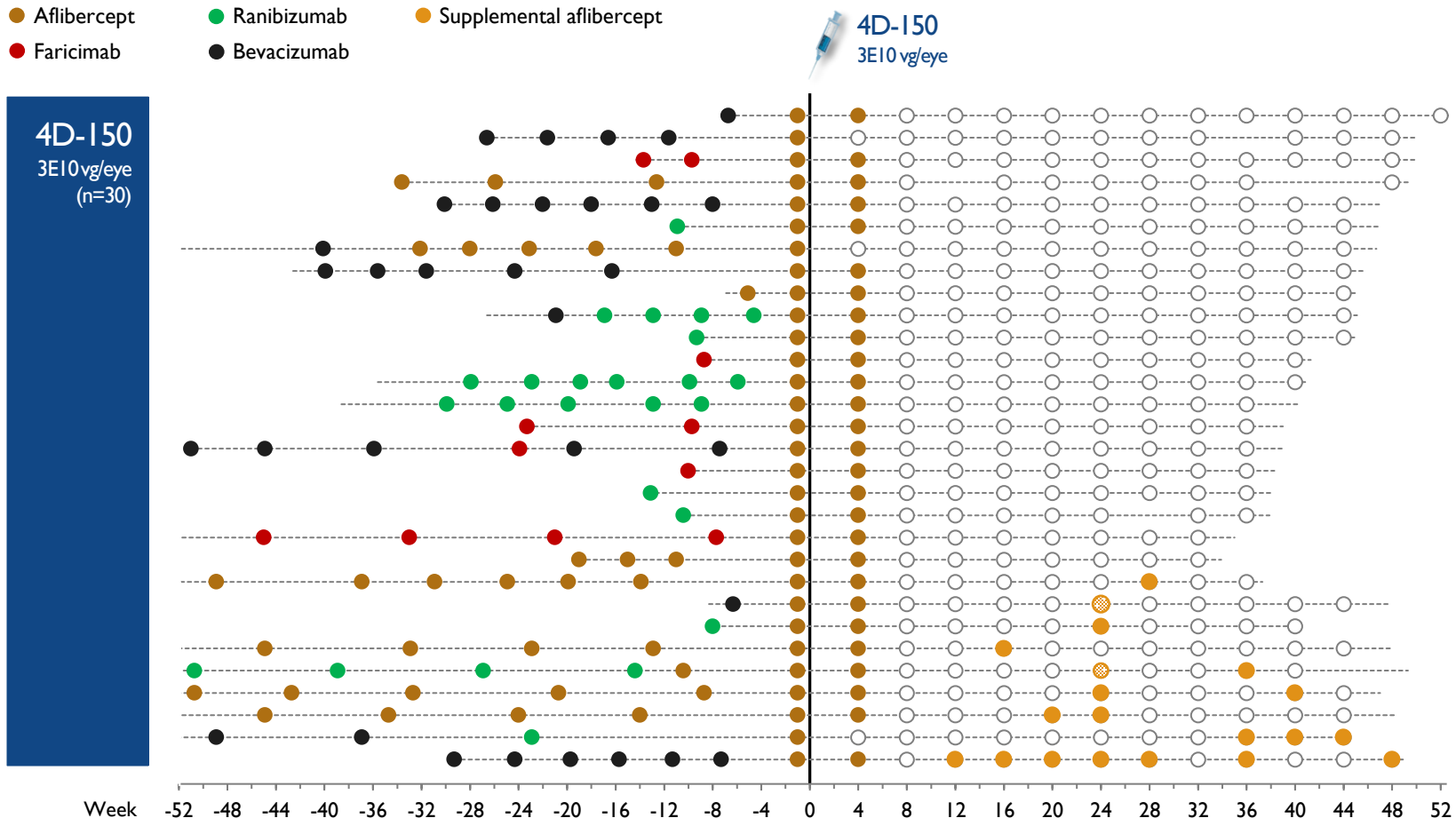
Data Cutoff Date: September 3, 2024

Efficacy Data Analyses:

Supplemental Injections

BCVA & CST

Phase 2b (3E10 vg/eye): 70% of Participants Remained Injection-free During Follow-up Ranging from 32 to 52 Weeks (Kaplan-Meier Estimate)



Supplemental Injections*

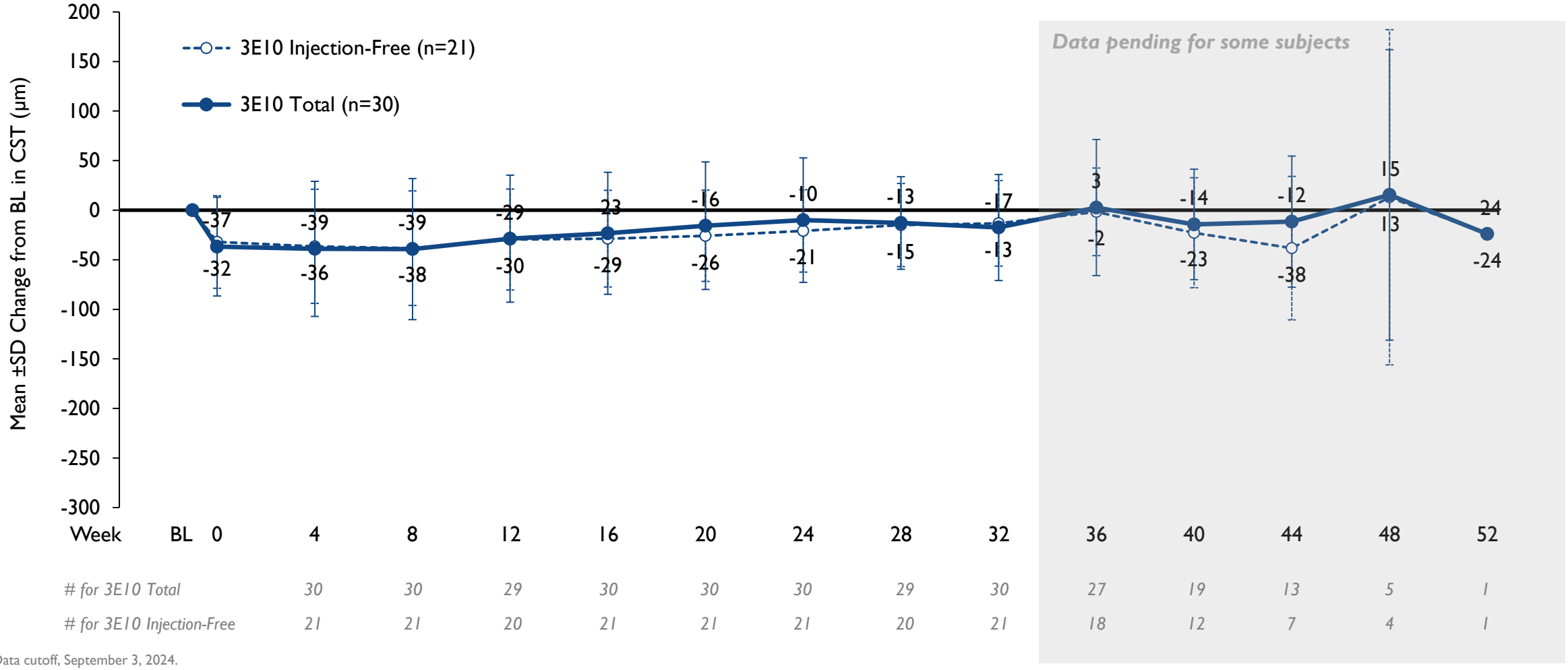
Status	Week 32	Week 52
Injection-free	73%	70%
0-1 injection	93%	80%

*Kaplan-Meier estimates

Data cutoff, September 3, 2024.

Supplemental injection administered based on investigator discretion (protocol-defined visual and anatomic criteria not met).

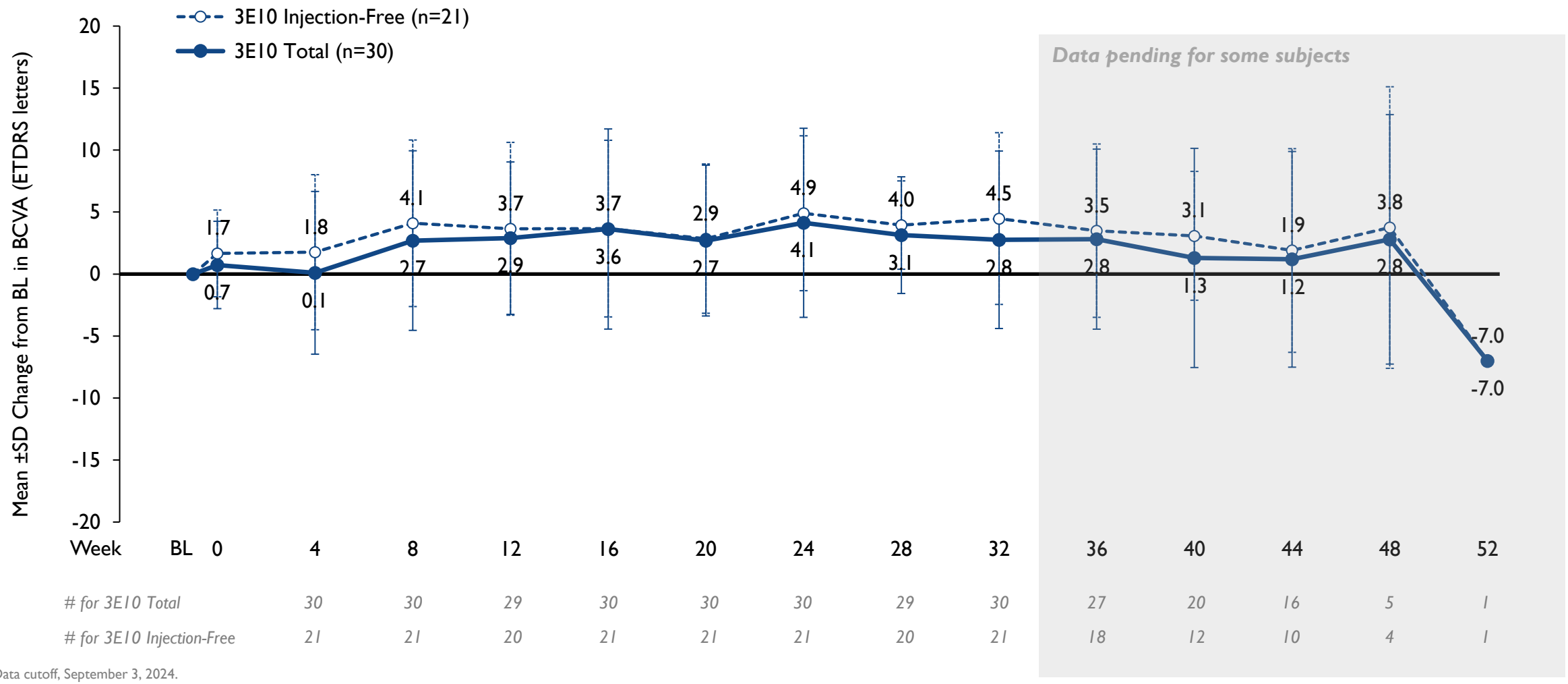
Phase 2b: Sustained Anatomic Control With Minimal Fluctuations



Week	BL	0	4	8	12	16	20	24	28	32	36	40	44	48	52
# for 3E10 Total			*30*	*30*	*29*	*30*	*30*	*30*	*29*	*30*	*27*	*19*	*13*	*5*	*1*
# for 3E10 Injection-Free			*21*	*21*	*20*	*21*	*21*	*21*	*20*	*21*	*18*	*12*	*7*	*4*	*1*

Data cutoff, September 3, 2024.
Baseline=Day -7. CST, central subfield thickness.

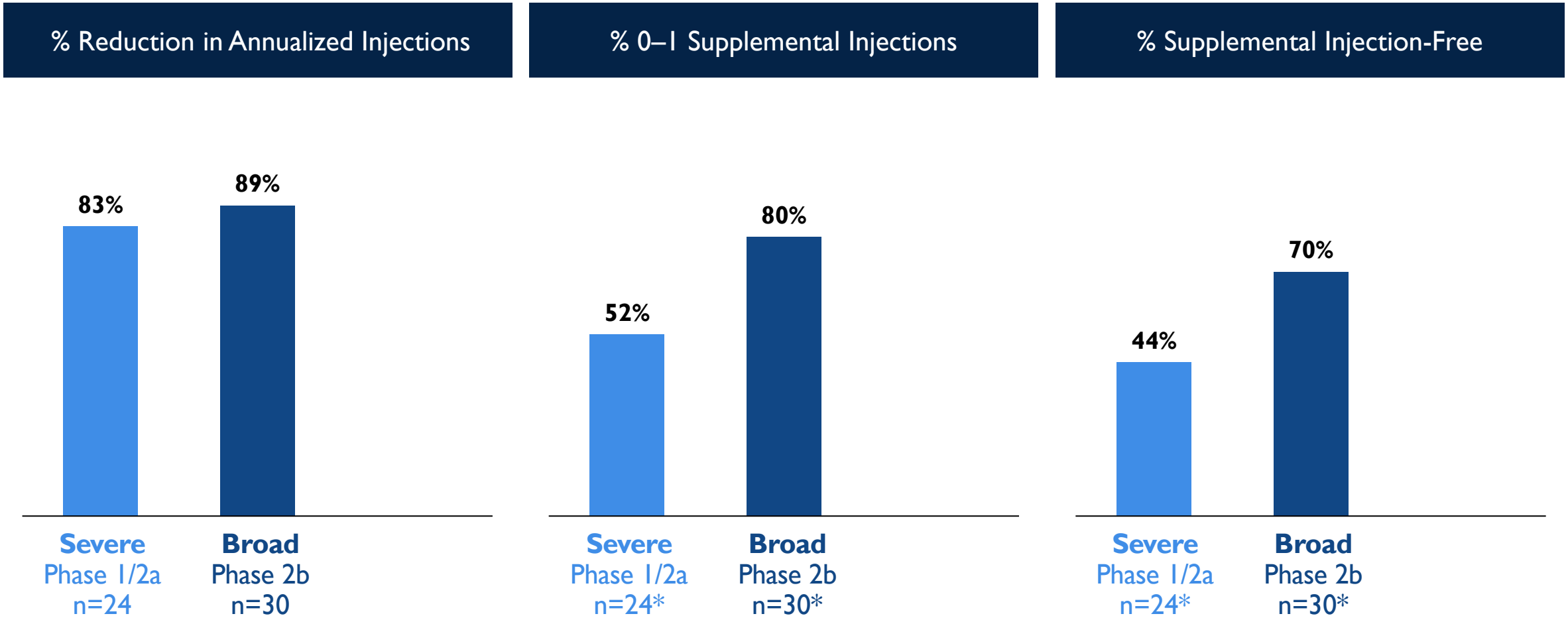
Phase 2b: Visual Acuity Improved and Stable



Week	BL	0	4	8	12	16	20	24	28	32	36	40	44	48	52
# for 3E10 Total			*30*	*30*	*29*	*30*	*30*	*30*	*29*	*30*	*27*	*20*	*16*	*5*	*1*
# for 3E10 Injection-Free			*21*	*21*	*20*	*21*	*21*	*21*	*20*	*21*	*18*	*12*	*10*	*4*	*1*

Data cutoff, September 3, 2024.
Baseline=Day -7. BCVA, best corrected visual acuity.

Robust & Durable Reduction in Treatment Burden in Broad Wet AMD Population **Through 52 Weeks** (Phase 3 Dose: 3E10 vg/eye)



Data cutoff, September 3, 2024.
*Based on Kaplan-Meier method for calculating endpoint with variable follow-up through 32-52 weeks.

Phase 2b:

Recently Diagnosed (≤6 months)

Follow-up: Through up to 52 weeks

4D-150 3E10 vg/eye (N=15)

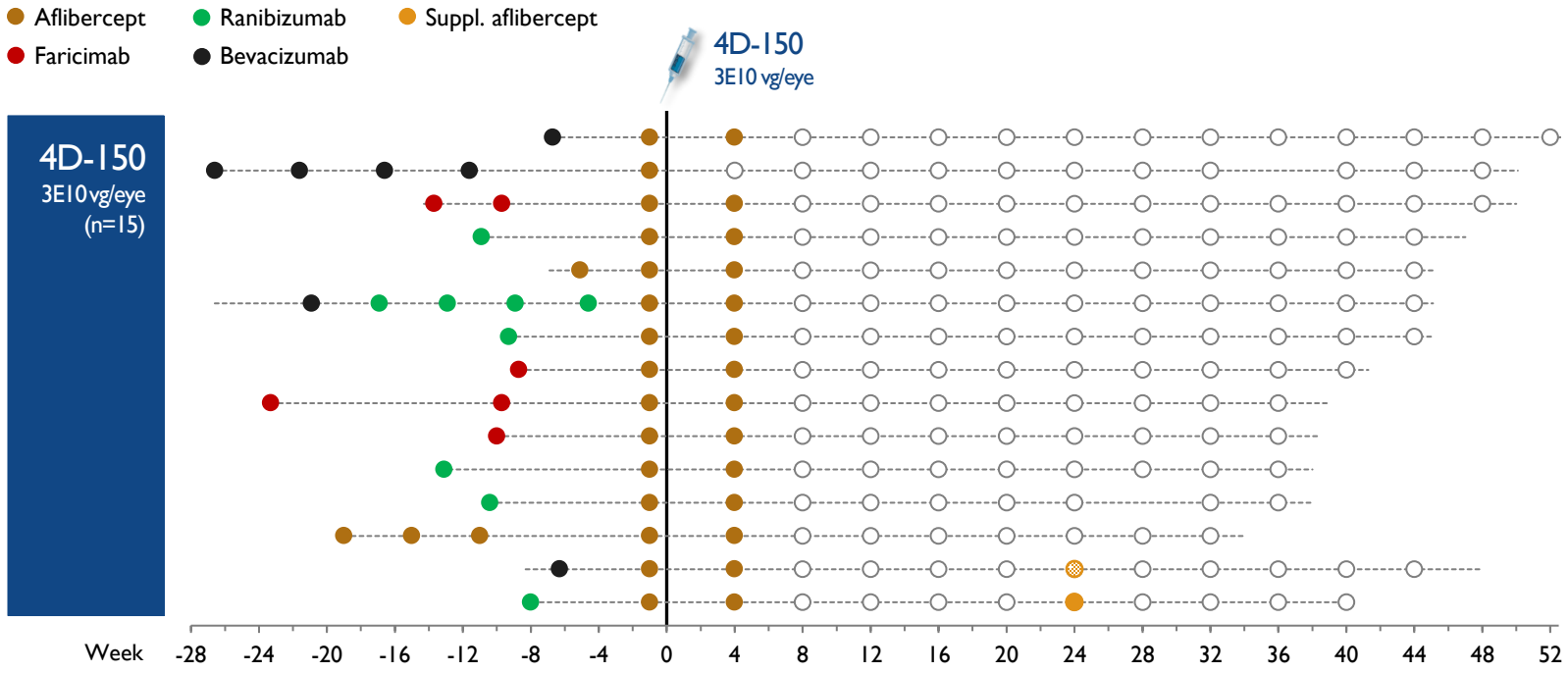
Data Cutoff Date: September 3, 2024

Efficacy Data Analyses:

Supplemental Injections

BCVA & CST

Phase 2b Recently Diagnosed: 87% Injection-free



Supplemental Injections*

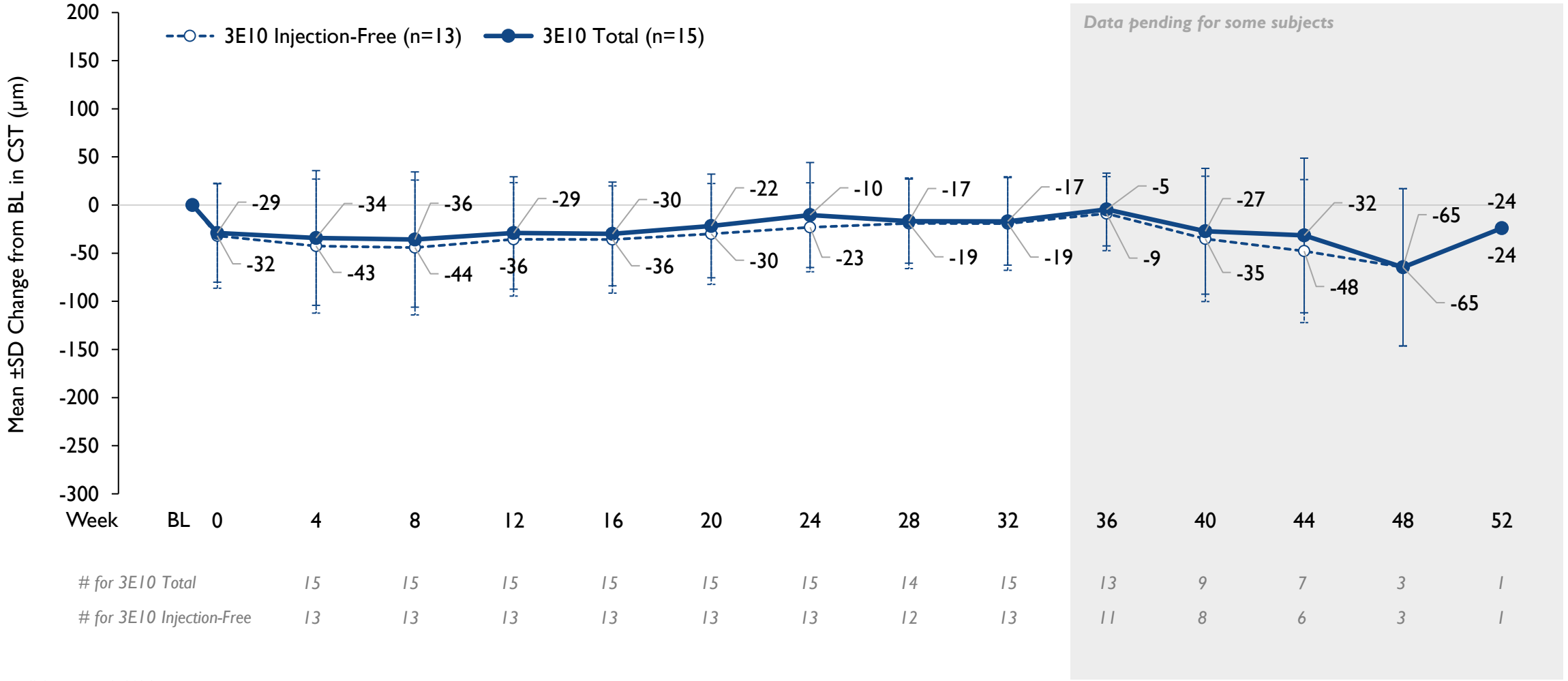
Status	Week 32	Week 52
Injection-free	87%	87%
0-1 injection	100%	100%

*Kaplan-Meier estimates

Data cutoff, September 3, 2024.

Supplemental injection administered based on investigator discretion (protocol-defined visual and anatomic criteria not met).

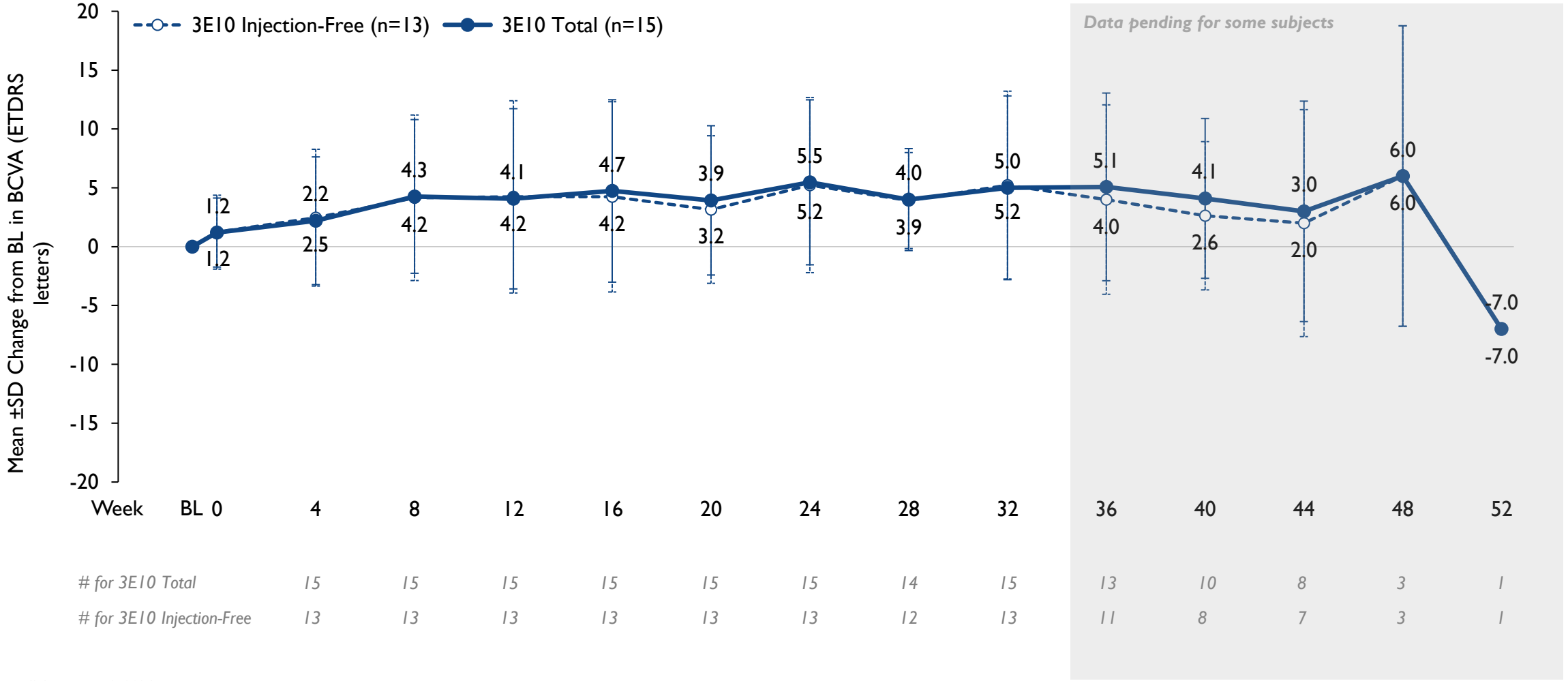
Phase 2b Recently Diagnosed: Sustained Anatomic Control With Fewer Fluctuations



Week	BL	0	4	8	12	16	20	24	28	32	36	40	44	48	52
# for 3E10 Total			*15*	*15*	*15*	*15*	*15*	*15*	*14*	*15*	*13*	*9*	*7*	*3*	*1*
# for 3E10 Injection-Free			*13*	*13*	*13*	*13*	*13*	*13*	*12*	*13*	*11*	*8*	*6*	*3*	*1*

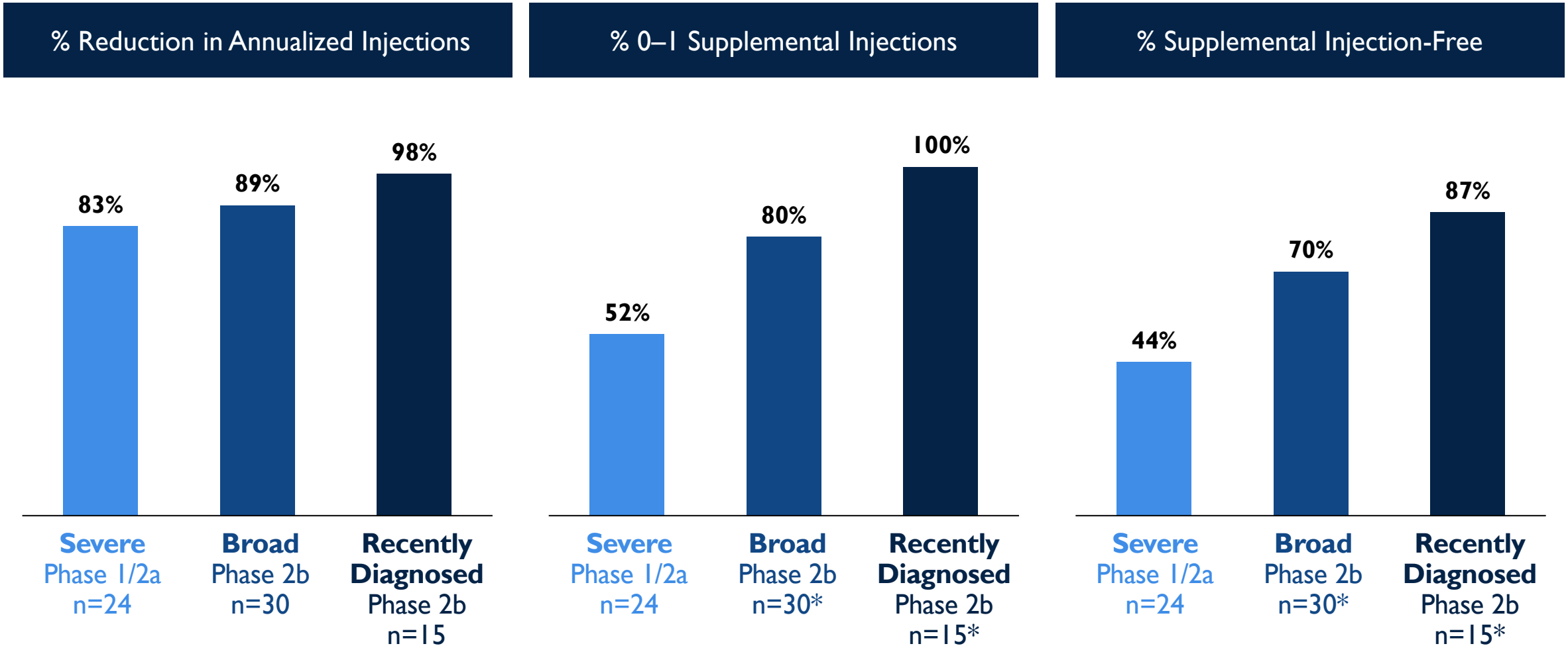
Data cutoff, September 3, 2024.
Baseline=Day -7. CST, central subfield thickness.

Phase 2b Recently Diagnosed: Visual Acuity Improved and Stable



Data cutoff, September 3, 2024.
Baseline=Day -7. BCVA, best corrected visual acuity.

Robust & Durable Reduction in Treatment Burden Across **All Wet AMD Populations** Studied **Through 52 Weeks** (Phase 3 Dose: 3E10 vg/eye)



Data cutoff, September 3, 2024.
Recently diagnosed group includes patients with ≤6 months disease duration.
*Based on Kaplan-Meier method for calculating endpoint with variable follow-up through 32-52 weeks.

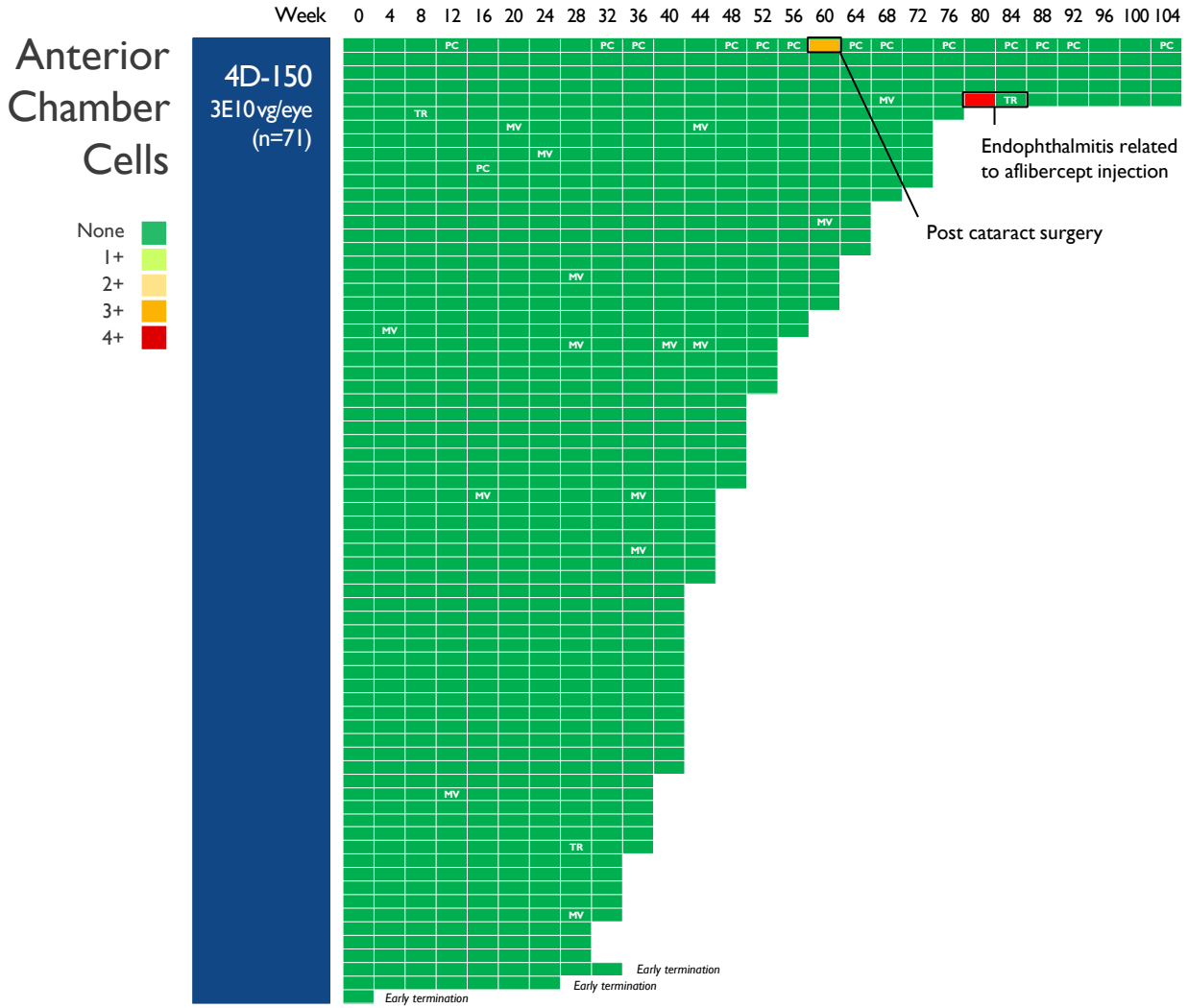
Phase 1/2a & 2b Interim Safety Data

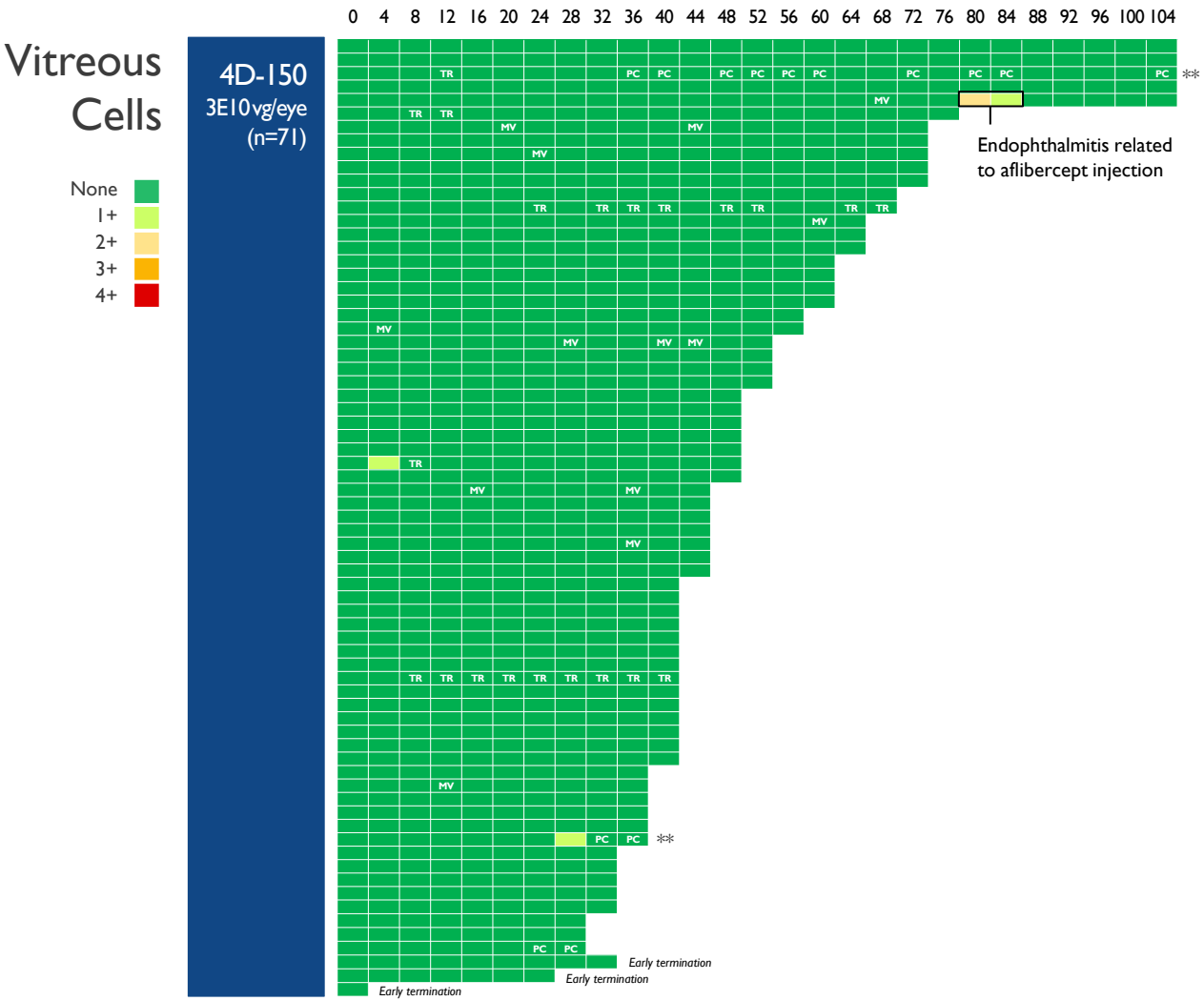
Follow-up: Through up to 130 weeks

4D-150 1E10 and 3E10 vg/eye (N=112)

Data Cutoff Date: August 23, 2024

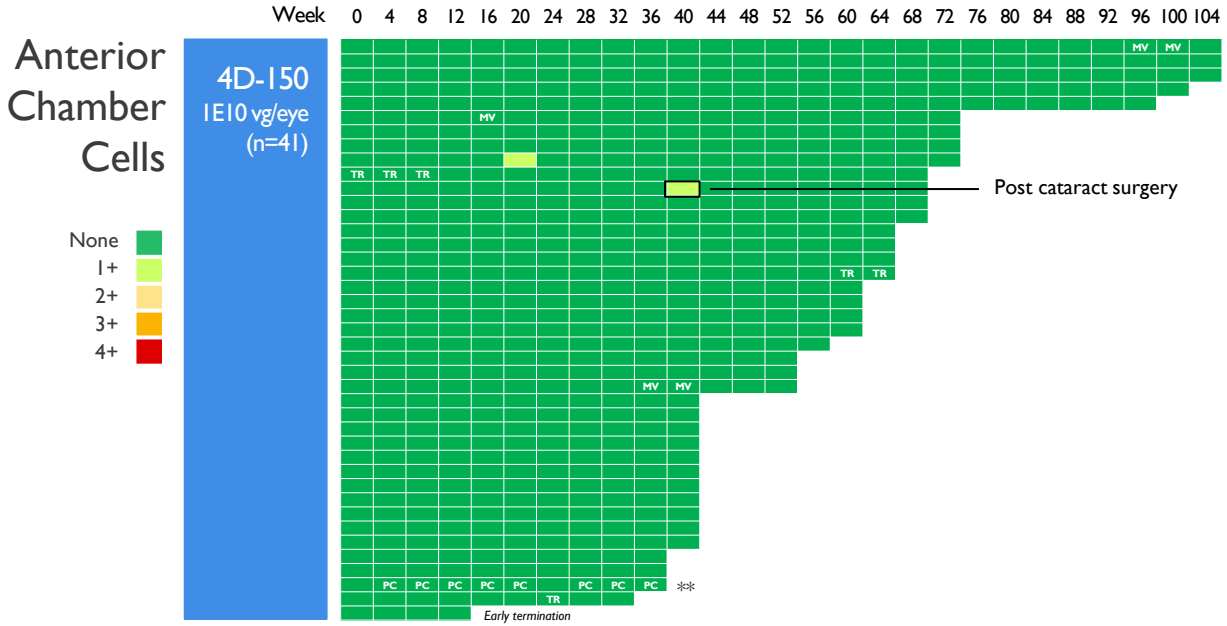
Ophthalmic Examination*: 4D-150 Continues to be Safe and Well Tolerated Across All Doses and Cohorts

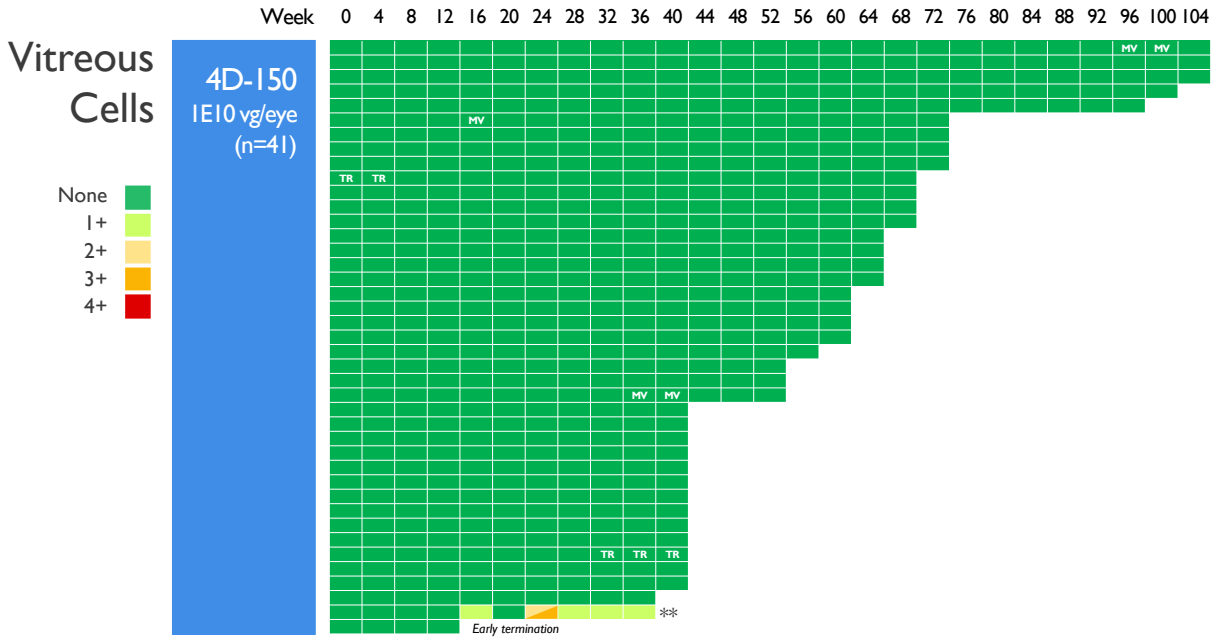




Date cutoff date: August 23, 2024.
*SUN and NEI Scores for white blood cells.
NEI, National Eye Institute; MV, missed visit; PC, pigmented cells; TR, trace; SUN, Standardization of Uveitis Nomenclature.; ** on topical steroids

Ophthalmic Examination*: 4D-150 Continues to be Safe and Well Tolerated Across All Doses and Cohorts





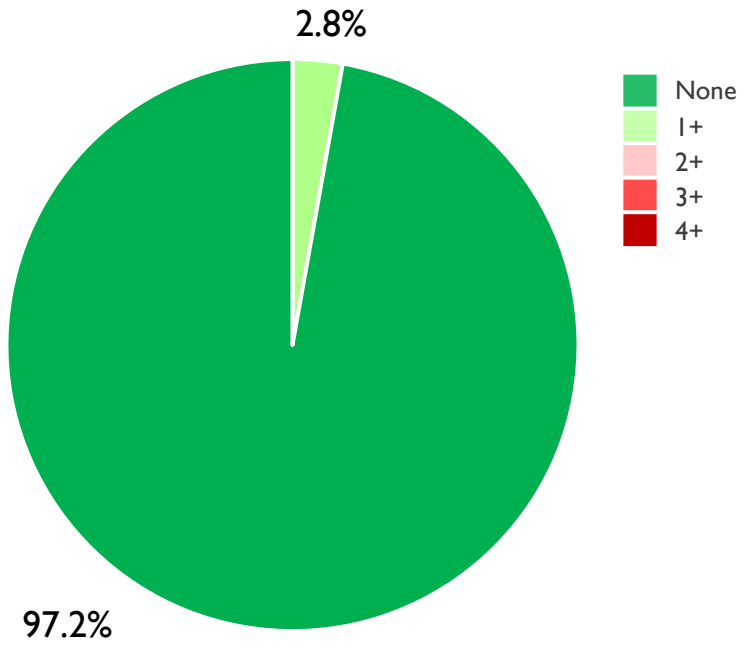
Date cutoff date: August 23, 2024.
*SUN and NEI Scores for white blood cells.
NEI, National Eye Institute; MV, missed visit; PC, pigmented cells; TR, trace; SUN, Standardization of Uveitis Nomenclature. ** on topical steroids

4D-150 Continues to be Well Tolerated

- No 4D-150–related serious adverse events
- Rate of 3E10 dose 4D-150–related intraocular inflammation: **Wet AMD**
  - **2.8%** (2 of 71) had transient 1+VC at any timepoint
  - **99%** (70 of 71) completed steroid prophylaxis taper on schedule
  - **97%** (69 of 71) remained off steroids completely
- No 4D-150–related hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions observed to date
  - Supplemental aflibercept injection–related case of endophthalmitis (presumed bacterial infection), resolved over following 2 visits
- Rate of intraocular inflammation: **DME**
  - **0%** treated at any dose (n=22) had IOI at any timepoint

All 4D-150 3E10 vg/eye-Treated Wet AMD Patients (N=71)

*Highest SUN/NEI Score (4D-150–Related)**



Data cutoff, August 23, 2024.
*Duration of follow up, ≤2.5 years. NEI, National Eye Institute; SUN, Standardization of Uveitis Nomenclature.

4D-150 PRISM Phase 1/2 Summary: All Patient Populations

1. **Treatment burden reduction: Robust & durable through up to 2.5 years**
2. **CST response: Strong & sustained anatomic control with fewer fluctuations**
3. **BCVA response: Stable or improved**
4. **Safety profile: Well-tolerated with profile numerically comparable to approved anti VEGFs***
5. **Supports advancement into Phase 3**

Data cutoff (clinical activity data), September 3, 2024.
Data cutoff (safety data), August 23, 2024.
* No head-to-head studies have been done

2024 4D-150 Wet AMD Development Day Agenda

1	**4DMT Overview & Key Takeaways** David Kirn, CEO	6	**Phase 3 4FRONT Program Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology
2	**Wet AMD & 4D-150 Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology	7	**4FRONT Discussion** *Moderator*: Dhaval Desai, CDO
3	**Phase 1/2 PRISM Overview** Robert Kim, CMO	8	**Preliminary Commercial Considerations** Christopher Simms, CCO
4	**Phase 1/2 PRISM Interim Data** Dhaval Desai, CDO	9	**Summary & Takeaways** David Kirn, CEO
5	**PRISM Discussion** *Moderator*: Dhaval Desai, CDO	10	**Audience Q&A** All

PRISM Discussion

Dhaval Desai, PharmD
Chief Development Officer

Arshad Khanani, MD, MA, FASRS
Director of Clinical Research at Sierra Eye Associates

Carl D. Regillo, MD, FACS, FASRS
Wills Eye Hospital

Dante Pieramici, MD
California Retina Consultants

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4FRONT Phase 3 Program in Treatment Naïve Wet AMD Population

Design Maximizes Probabilities of Clinical, Regulatory & Commercial Success

1

Informed by:

- PRISM interim data
- Phase 3 designs of marketed intravitreal anti-VEGF products
- Regulatory discussions with FDA & EMA under RMAT & PRIME

2

Goals:

- Maximize probability of success for:
  - Primary endpoint: BCVA non-inferiority
  - Secondary endpoint: treatment burden reduction
  - Commercialization

3

Design features:

- Anti-VEGF responsive on study to be randomized
- 4D-150 3E10 vg/eye dose
- Durezol topical eyedrops
- 3 monthly loading doses applied to both arms
- Comparator arm 2Q8W dosing without supplemental injections

4FRONT-1 Phase 3 Wet AMD Study Design

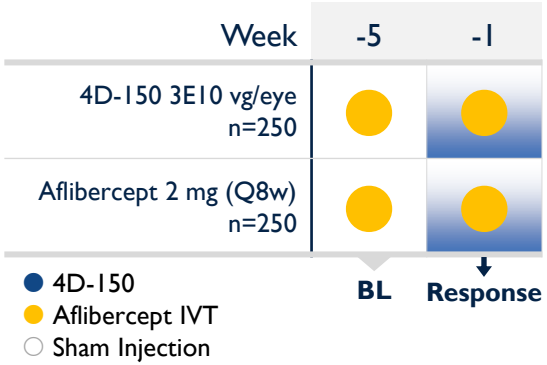
Population Enriched to Maximize Clinical Outcomes

Key Inclusion Criteria

Treatment naïve wet AMD

BCVA:
25-78 letters

Anti-VEGF responsive:
After Week -5 loading dose



4FRONT-1 Phase 3 Wet AMD Study Design

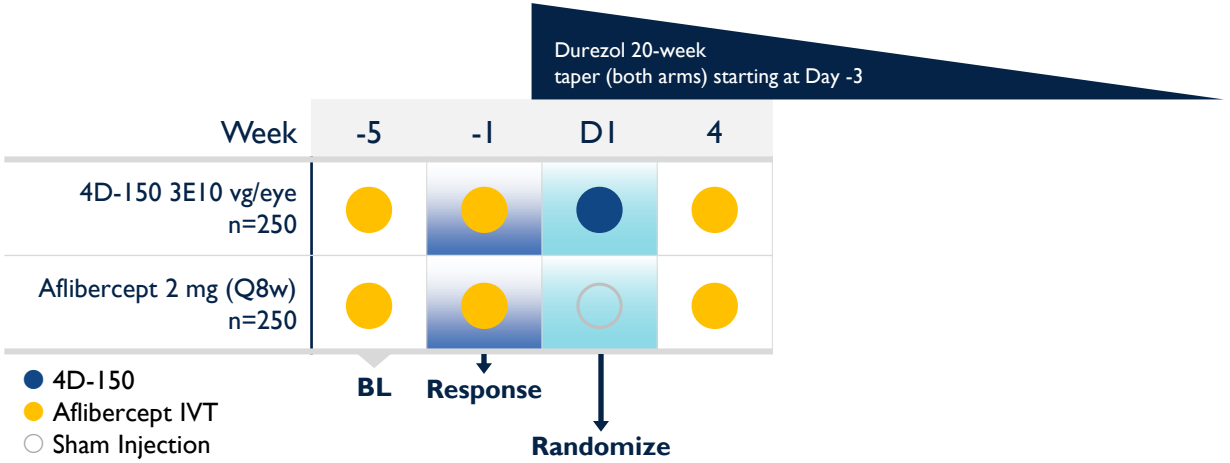
Patients are Randomized and Receive 3 Total Aflibercept Loading Doses per Label

Key Inclusion Criteria

Treatment naïve wet AMD

BCVA:
25-78 letters

Anti-VEGF responsive:
After Week -5 loading dose



4FRONT-1 Phase 3 Wet AMD Study Design

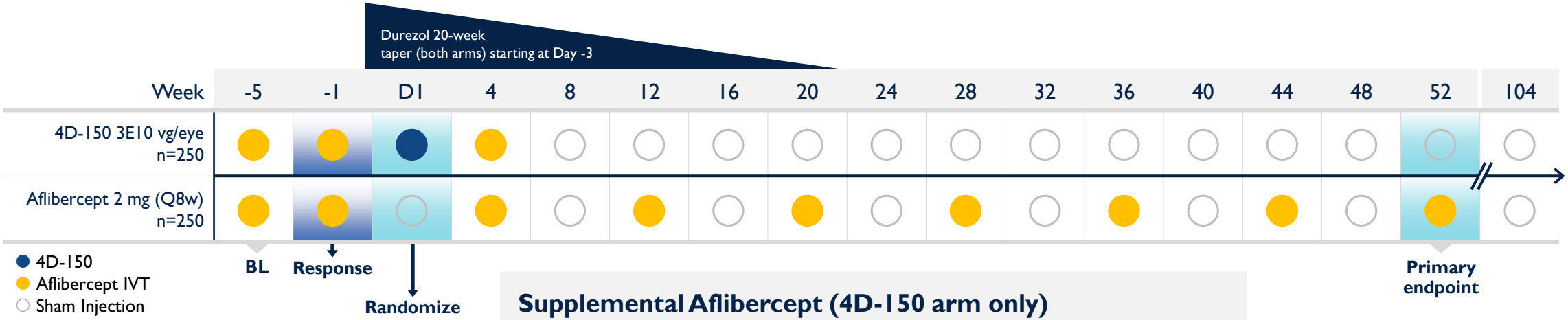
Supplemental Criteria Applied Based on Reference Point After 3 Aflibercept Loading Doses

Key Inclusion Criteria

Treatment naïve wet AMD

BCVA:
25-78 letters

Anti-VEGF responsive:
After Week -5 loading dose



Supplemental Aflibercept (4D-150 arm only)

Reference Point:
After 3 loading doses

Pre-specified criteria for BCVA & CST worsening to maintain BCVA and **protect primary endpoint**

Designed to Drive Clinical, Regulatory & Commercial Success

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4FRONT Discussion

Dhaval Desai, PharmD

Chief Development Officer

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Director of Clinical Research at Sierra Eye Associates

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Wills Eye Hospital

Dante Pieramici, MD

California Retina Consultants

4FRONT-1 Phase 3 Wet AMD Study Design

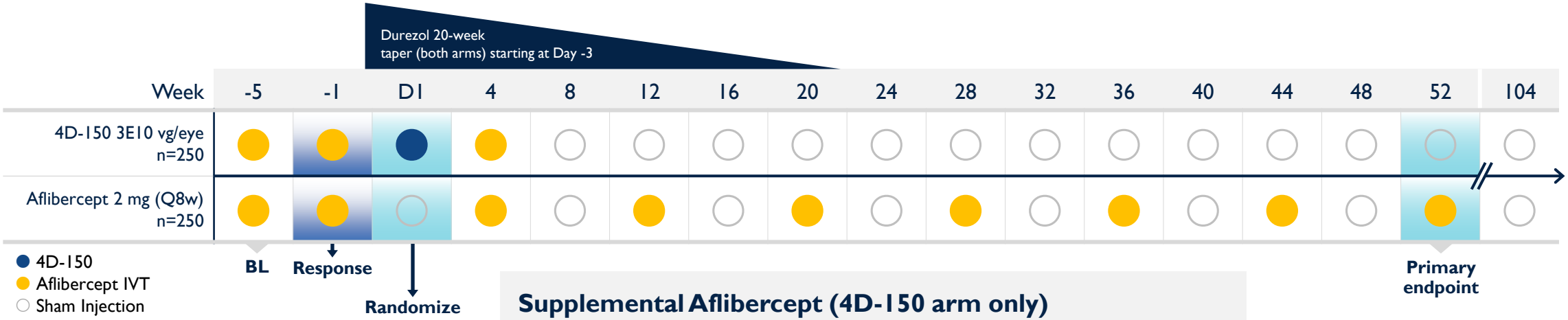
Primary Endpoint: BCVA Noninferiority of 4D-150 3E10 vg/eye to Aflibercept 2mg Q8 weeks

Key Inclusion Criteria

Treatment naïve wet AMD

BCVA: 25-78 letters

Anti-VEGF responsive: After Week -5 loading dose



Supplemental Aflibercept (4D-150 arm only)

Reference Point: After 3 loading doses

Pre-specified criteria for BCVA & CST worsening to maintain BCVA and **protect primary endpoint**

Designed to Drive Clinical, Regulatory & Commercial Success

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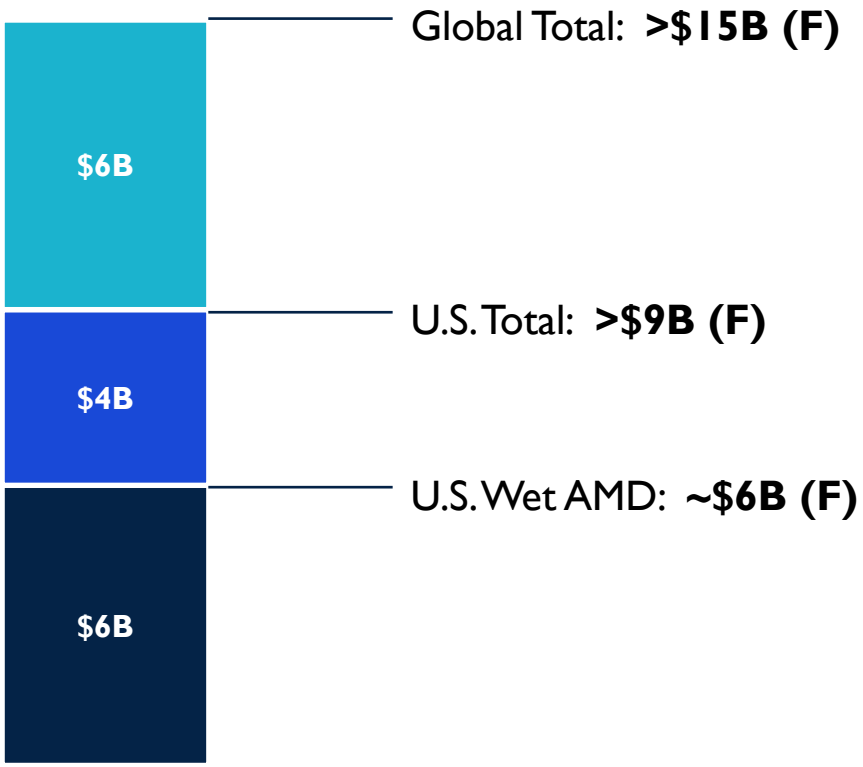
U.S. Wet AMD Market is ~$6B Today and Will Continue to Grow

2024 Branded Ocular Anti-VEGF Market

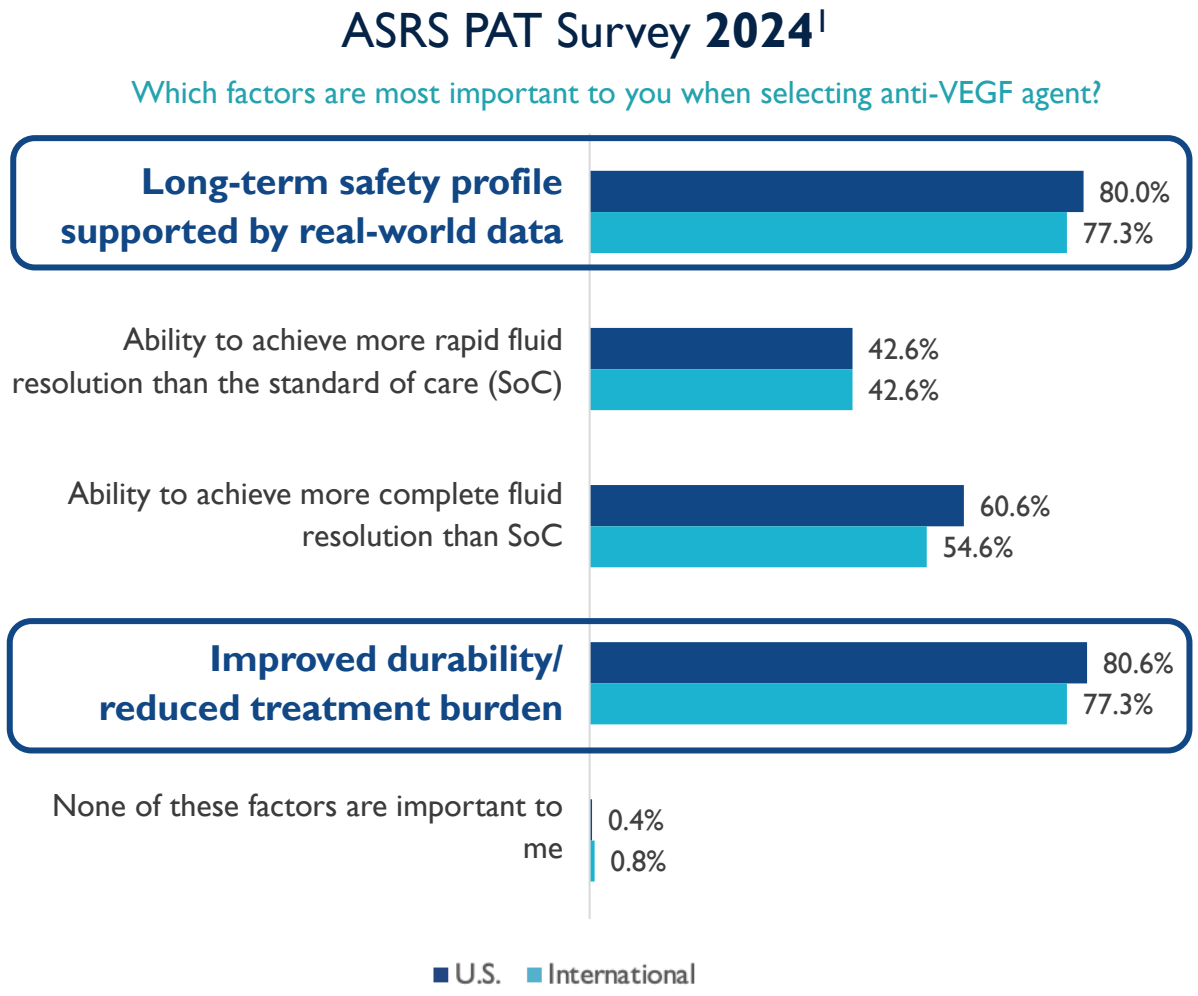


Wet AMD Population Estimates (U.S., 2024)

1.65M	Prevalence
>200K	Annual Incidence
~3%	Population Growth (65+)

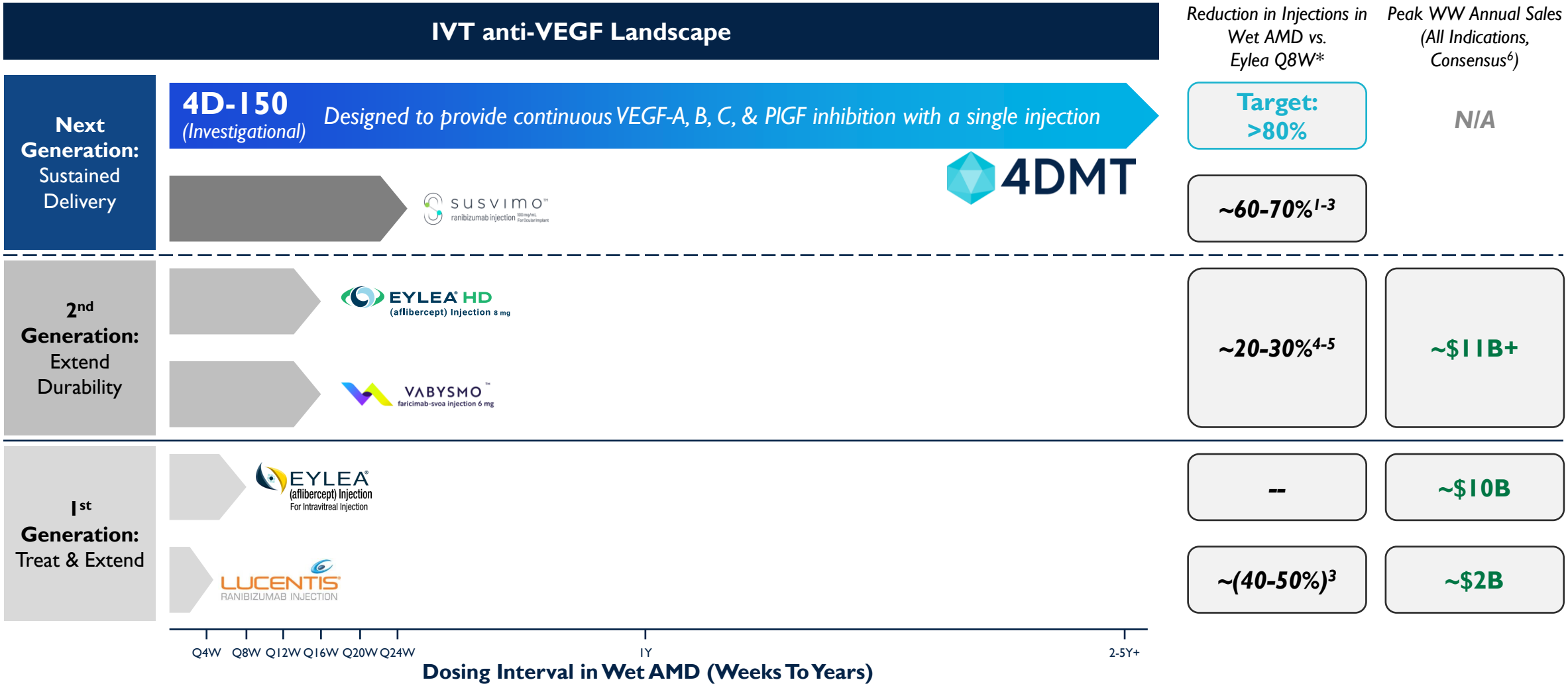
Sources: For anti-VEGF market - GlobalData, GrandView Research.
Annual incidence derived from analysis of key publications (Vanderbeek 2011, Rudnicka 2015, Klein 2011 and Fisher 2016), triangulated with IQVIA claims data; population growth calculated from U.S. census projections for ages 65+ in the U.S.
Prevalence sourced from Marketscope Retina Market Report 2023; (F) = forecast for 2024

Largest Unmet Need in Wet AMD is Durable Efficacy with a Safe Treatment, Despite Recent Approvals of 2nd Generation Anti-VEGFs



1. Han P, ASRS 2024 PAT Survey. PAT, Preferences and Trends.

Potential for Transformative Profile that Unlocks Blockbuster Markets



Mean no. of injections over Year 0-2: Susvimo (ARCHWAY) vs. Eylea Q8W (VIEW 1 & 2) 2. Regillo et al. *Ophthalmology* 2023; 130:735-7 (ARCHWAY). 3. Schmidt-Erfurth et al. *Ophthalmology* 2014; 121:193-201 (VIEW 1 & 2) 4. Eylea HD: Regeneron publicly available information/company website as of 8/10/23 (PULSAR data) 5. Vabysmo: CDER statistical review; Khanani et al., *Ophthalmology* 2024; 1-13 (TENAYA and LUCERNE) 6. FactSet 2028E WW sales for Eylea HD and Vabysmo; FactSet for Eylea and Lucentis peak WW sales *The data presented above are based on cross-study comparisons and are not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

4D-150 Opportunity Grounded in Meeting Needs of All Stakeholders

Target Product Profile

Safety comparable to market leading anti VEGF brands

Efficacy that Maximizes Visual Outcomes with Extended Durability

In-Office, Intravitreal Administration

Patients

- Efficacious and safe treatment
- Significant reduction in treatment burden
- Potential for better outcomes with sustained disease control

Physicians

- Efficacious and safe treatment for broad AMD patient base
- Significant reduction in treatment burden helps create practice capacity
- IVT delivery that supports current practice logistics and reimbursement (buy & bill)

Payers

- Improved patient adherence to therapy, leading to improved preservation of vision gains
- Population level reduction in treatment burden
- Socio-economic benefit from reduction in vision impairment

2024 4D-150 Wet AMD Development Day Agenda

1	**4DMT Overview & Key Takeaways** David Kirn, CEO	6	**Phase 3 4FRONT Program Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology
2	**Wet AMD & 4D-150 Overview** Carlos Quezada-Ruiz, SVP, TAH, Ophthalmology	7	**4FRONT Discussion** *Moderator*: Dhaval Desai, CDO
3	**Phase 1/2 PRISM Overview** Robert Kim, CMO	8	**Preliminary Commercial Considerations** Christopher Simms, CCO
4	**Phase 1/2 PRISM Interim Data** Dhaval Desai, CDO	9	**Summary & Takeaways** David Kirn, CEO
5	**PRISM Discussion** *Moderator*: Dhaval Desai, CDO	10	**Audience Q&A** All

Key 4D-150 Takeaways in Wet AMD

1. **Robust & Durable Clinical Activity:** Across all populations studied, including recently diagnosed patients

2. **Tolerability:** Well-tolerated with profile comparable to approved anti-VEGF agents

3. **4FRONT Phase 3 Design:** Maximizes probabilities of clinical, regulatory & commercial success

Data cutoff (clinical activity data), September 3, 2024.
Data cutoff (safety data), August 23, 2024.

Rapidly Advancing Development in Large Market Ophthalmology Indications with the R100 Platform

VECTOR DELIVERY	PRODUCT CANDIDATE	INDICATION	EPIDEMIOLOGY (PREVALENCE)	PHASE 1	PHASE 2	PHASE 3	MILESTONES
LARGE MARKET OPHTHALMOLOGY **R100** **Intravitreal** 	**4D-150** Aflibercept + VEGF-C RNAi	**Wet AMD**	*~3M U.S./EUMM*	4FRONT-1 4FRONT-2 PRISM			✓ Phase 2a 24-week Update (N=51) ✓ Phase 2b 24-week Update (N=45) ✓ **4D-150 Wet AMD Development Day** ✓ Interim Longest Available Data Phase 1/2a, 2b ✓ Final 4FRONT Phase 3 Design ▪ **Feb 25** Phase 2b 52-week update ▪ **Q1:25** Initiate Phase 3 4FRONT-1 clinical trial
		Diabetic Macular Edema	*~5M U.S./EUMM*	SPECTRA			▪ **Q4:24** Initial interim data from Phase 2a
	4D-175 Short Form Complement Factor H	**Geographic Atrophy**	*~2.5M U.S./EUMM*	GAZE			✓ IND Cleared June 2024 ▪ **Q4:24** Begin Phase 1 enrollment

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Here to Answer Your Questions

David Kirn, MD
Co-Founder & CEO

Robert Kim, MD
Chief Medical Officer

Dhaval Desai, PharmD
Chief Development Officer

Uneek Mehra
Chief Financial & Business Officer

Christopher Simms
Chief Commercial Officer

Carlos Quezada-Ruiz, MD, FASRS
SVP, Therapeutic Area Head, Ophthalmology

Arshad Khanani, MD, MA, FASRS
Director of Clinical Research at Sierra Eye Associates

Carl D. Regillo, MD, FACS, FASRS
Wills Eye Hospital

Dante Pieramici, MD
California Retina Consultants

THANK YOU

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4DMT

Appendix 1:

PRISM

Phase 1/2a Interim Data

Follow-up: Through up to 130 weeks

4D-150 3E10 vg/eye, 1E10 vg/eye & aflibercept control (N=60)

Data Cutoff Date, September 3, 2024

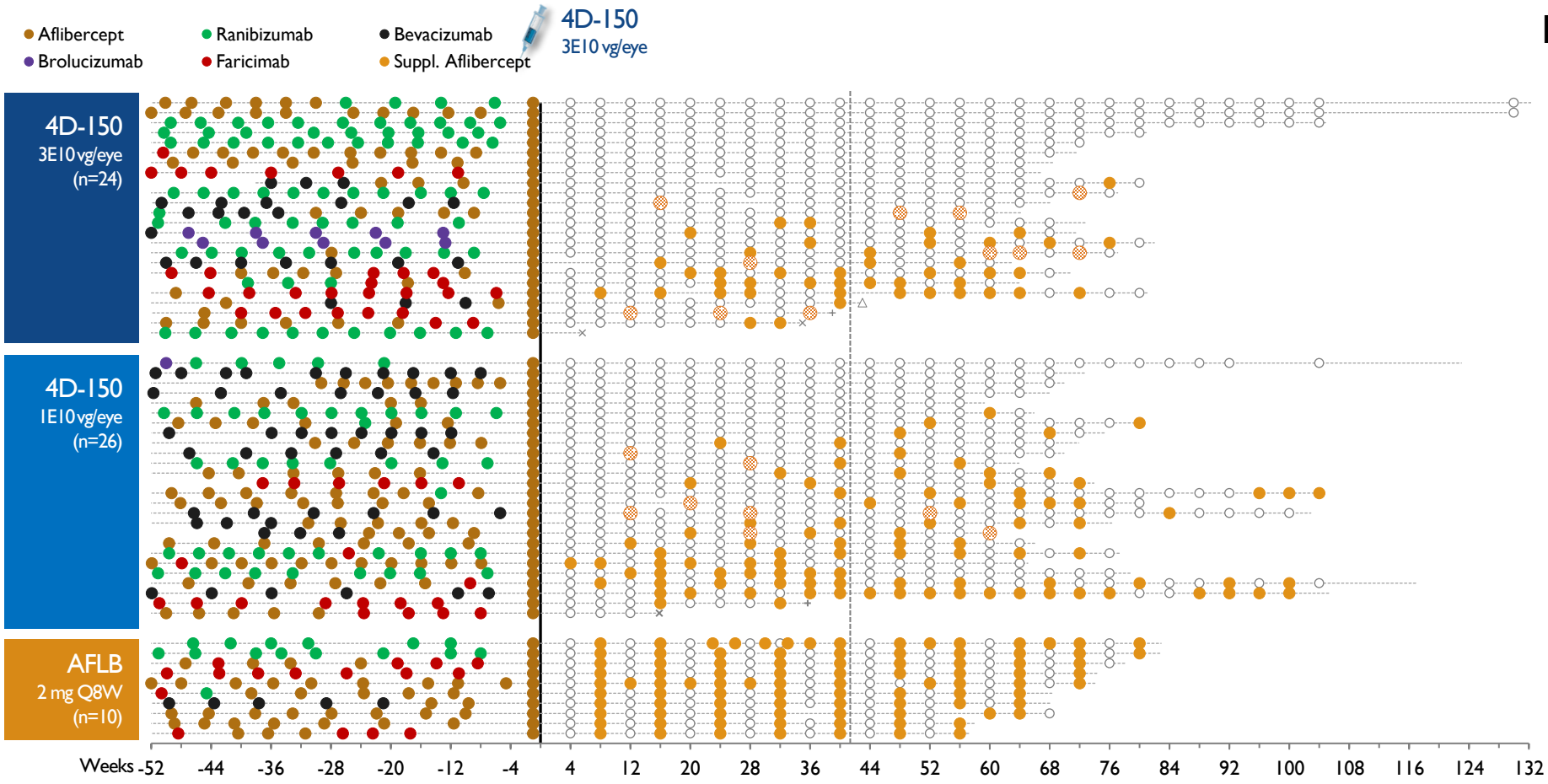
Baseline Characteristics: Phase 1/2a (Dose Exploration/Expansion)

Characteristic	4D-150 3E10 vg/eye N=24	4D-150 1E10 vg/eye N=26	AFLB 2mg Q8W N=10	All N=60
Mean ±SD age, years	77 ± 7.9 *59–91*	77 ± 8.6 *57–92*	80 ± 4.1 *74–85*	77 ± 7.7 *57–92*
Mean ±SD BCVA, ETDRS letters	67 ± 11.0 *35–80*	70 ± 11.7 *39–82*	71 ± 13.2 *43–87*	69 ± 12.5 *35–87*
Mean ±SD central subfield thickness, µm	425 ± 89.8 *302–742*	443 ± 114.5 *295–816*	419 ± 64.3 *326–521*	432 ± 97.1 *295–816*
Mean ±SD time since diagnosis, years	3.7 ± 2.9 *0.7–11.1*	2.9 ± 2.1 *0.7–8.2*	2.1 ± 1.5 *1.0–5.7*	3.1 ± 2.4 *0.7–11.1*
Mean prior *annualized* injection rate*	*10.1*	*9.7*	*9.0*	*9.7*
Mean ±SD *number* injections, prior 12 months*	10.2 ± 2.4 *7–13*	9.2 ± 2.1 *7–14*	9.3 ± 0.9 *8–11*	9.6 ± 2.1 *7–14*

- Phase 1 & 2a pooled for clinical activity analyses
- Previously reported BCVA outlier (legally blind prior to study) from Phase 1 3E10 vg/eye arm excluded from clinical activity analysis

*Includes Day -7 AFLB injection. BCVA, best corrected visual acuity; VEGF, vascular endothelial growth factor.

Phase 1/2a: Dose Response Observed Between High and Low Dose 4D-150



Reduction in Annualized Injection Rate:

–83%

–71%

–28%

Data cutoff, September 3, 2024.

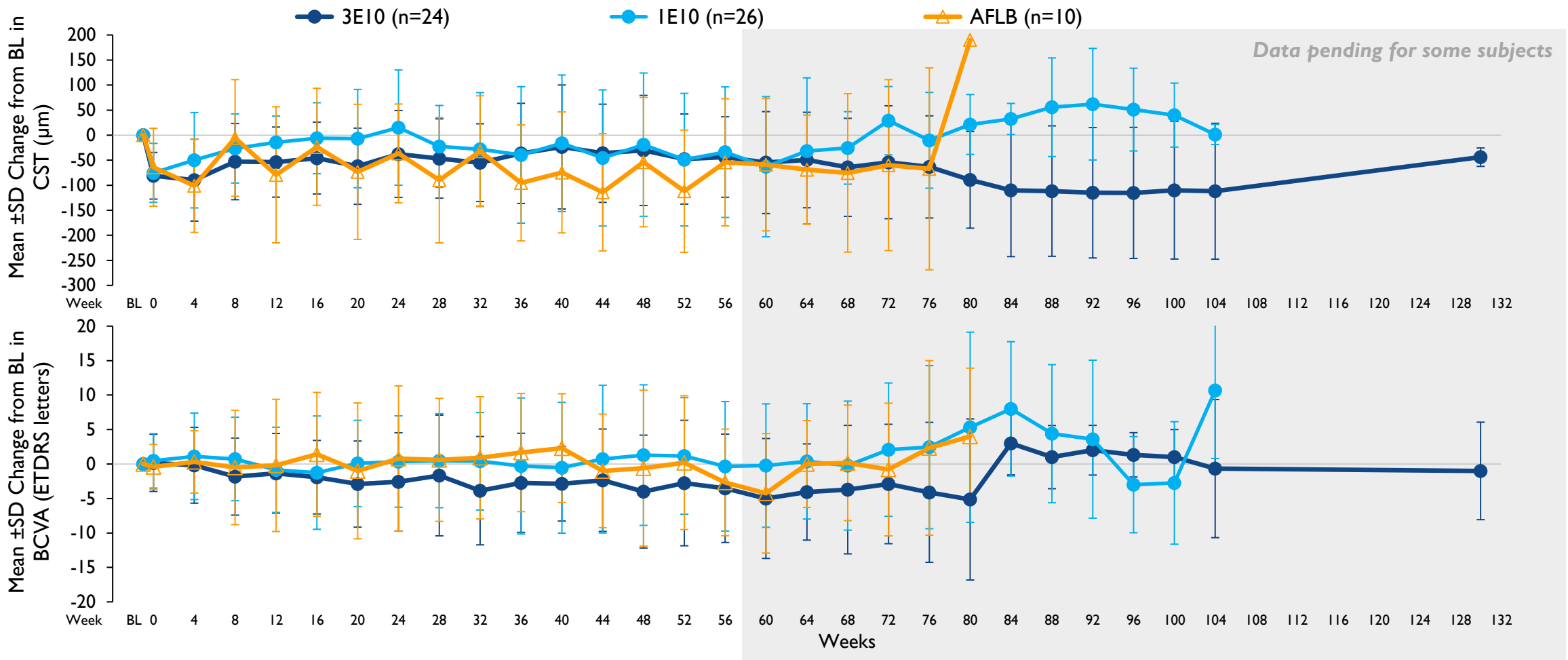
⊗ Supplemental injection administered based on investigator discretion (protocol-defined visual and anatomic criteria not met).

\+ Participant censored for supplemental injection assessment owing to protocol deviation (lost to follow up for >3 months after entering a nursing home).

× Early termination (death unrelated to study treatment), one of whom had missing data from Week 36 until death at Week 57.

Δ Subretinal macular hemorrhage at Week 41; PI elected to administer 5 consecutive doses of aflibercept (4-week dosing interval) while blood resorbed (i.e., no new/ongoing hemorrhage); all 5 aflibercept injections were included in the calculation of mean annualized anti-VEGF injections. PI subsequently converted to an 8-week aflibercept dosing schedule; however, criteria for supplemental injection were not present. At week 104, the mean change from baseline in BCVA was -1 letter and the mean change in CST was -71 μm.

Phase 1/2a: Visual Acuity and Anatomic Outcomes Equivalent to Aflibercept



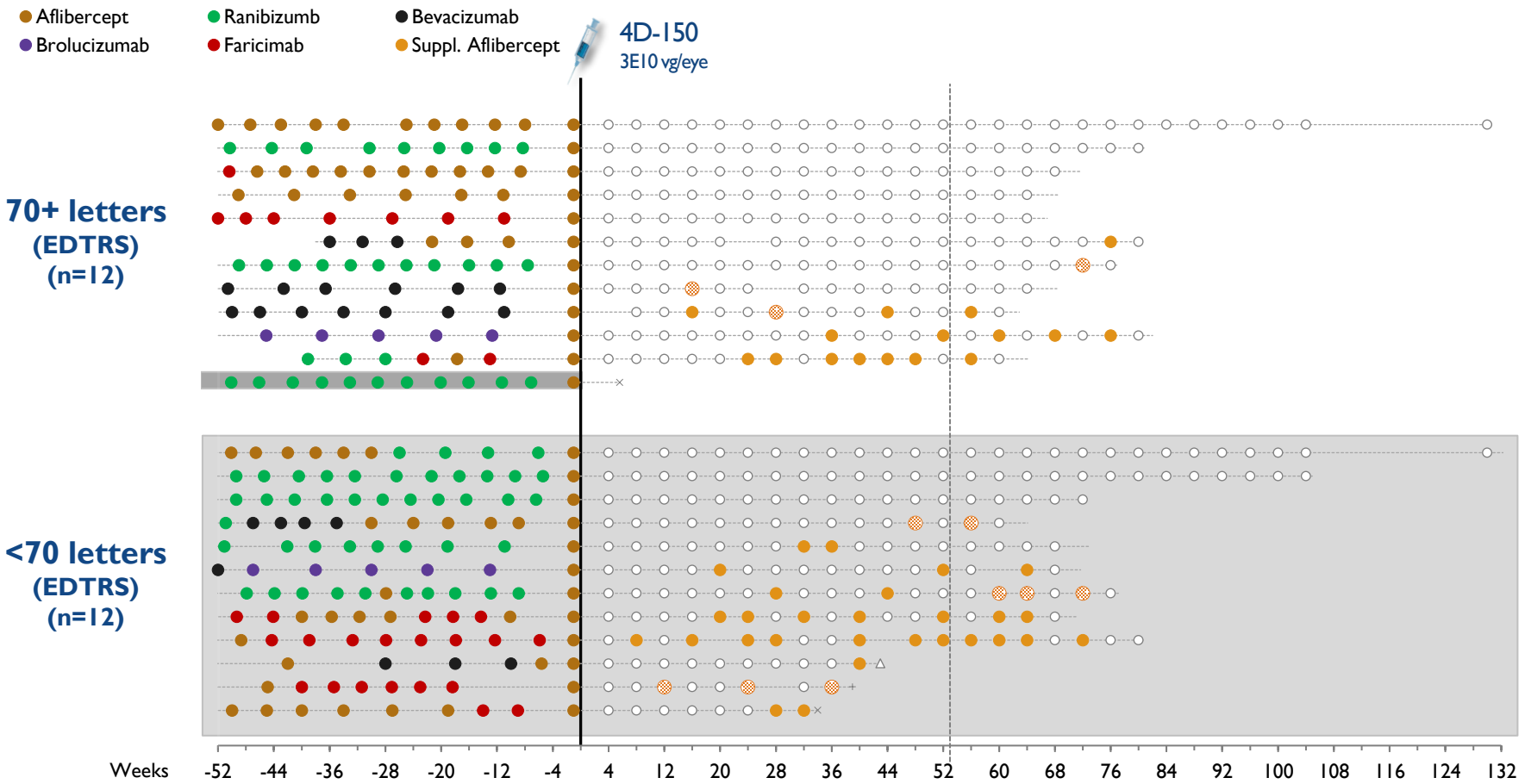
Data cutoff, September 3, 2024.
Baseline=Day -7. BCVA, best corrected visual acuity, CST, central subfield thickness.

Baseline Characteristics: BCVA Top 50% vs Lower 50% of All Patients in Phase 1/2a (≥70 Letters vs <70 Letters)

	3E10 vg/eye BCVA@BL <70 (N=12)	3E10 vg/eye BCVA@BL 70+ (N=12)
Mean ±SD age, years	75 ± 8.1 *59–89*	78 ± 7.7 *65–91*
Mean ±SD BCVA, ETDRS letters	59 ± 9.4 *35–69*	**76** ± 2.7 *73–80*
Mean ±SD central subfield thickness, μm	428 ± 121.9 *302–742*	422 ± 44.3 *342–495*
Mean ±SD time since diagnosis, years	3.4 ± 2.3 *1.0–7.5*	4.1 ± 3.4 *0.7–11.1*
Mean prior *annualized* injection rate*	*10.4*	*9.8*
Mean ±SD *number* injections, prior 12 months*	10.7 ± 2.3 *7–13*	9.5 ± 2.5 *7–13*

*Includes Day -7 AFLB injection. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation; VEGF, vascular endothelial growth factor.

Severe Patients With Maintained BCVA: Injection-Free Rate 64% & Injection Reduction 89%



Anti-VEGF Injections (Week 52)

BCVA Subgroup	Annualized Reduction	Supplemental Injections*		
		0–2	0–1	0
BCVA 70+ (n=12)	**89%**	**82%**	**73%**	**64%**

No injections per CST or BCVA criteria in 8 of 11 patients (73% through 72 weeks)

BCVA Subgroup	Annualized Reduction	Supplemental Injections*		
		0–2	0–1	0
BCVA <70 (n=12)	77%	65%	33%	25%

Data cutoff, September 3, 2024

⊗ Supplemental injection administered based on investigator discretion (protocol-defined visual and anatomic criteria not met).

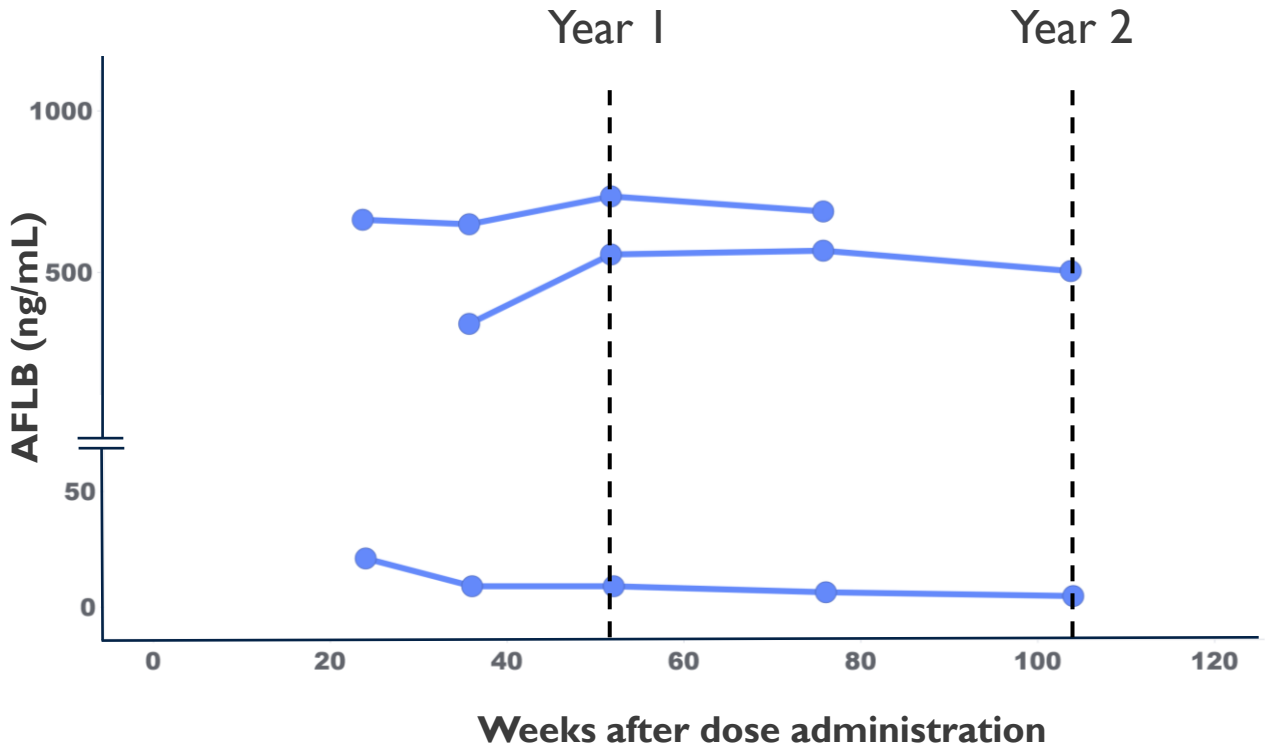
\+ Participant censored for supplemental injection assessment owing to protocol deviation (lost to follow up for >3 months after entering a nursing home).

× Early termination (death unrelated to study treatment), one of whom had missing data from Week 36 until death at Week 57.

Δ Subretinal macular hemorrhage at Week 41; PI elected to administer 5 consecutive doses of aflibercept (4-week dosing interval) while blood resorbed (i.e., no new/ongoing hemorrhage); all 5 aflibercept injections were included in the calculation of mean annualized anti-VEGF injections. PI subsequently converted to an 8-week aflibercept dosing schedule; however, criteria for supplemental injection were not present. At week 104, the mean change from baseline in BCVA was -1 letter and the mean change in CST was -71 μm.

Durable & Stable Serial Aflibercept Concentrations After 4D-150: Through 2 Years in All Injection-Free Phase 1 3E10 vg/eye Patients

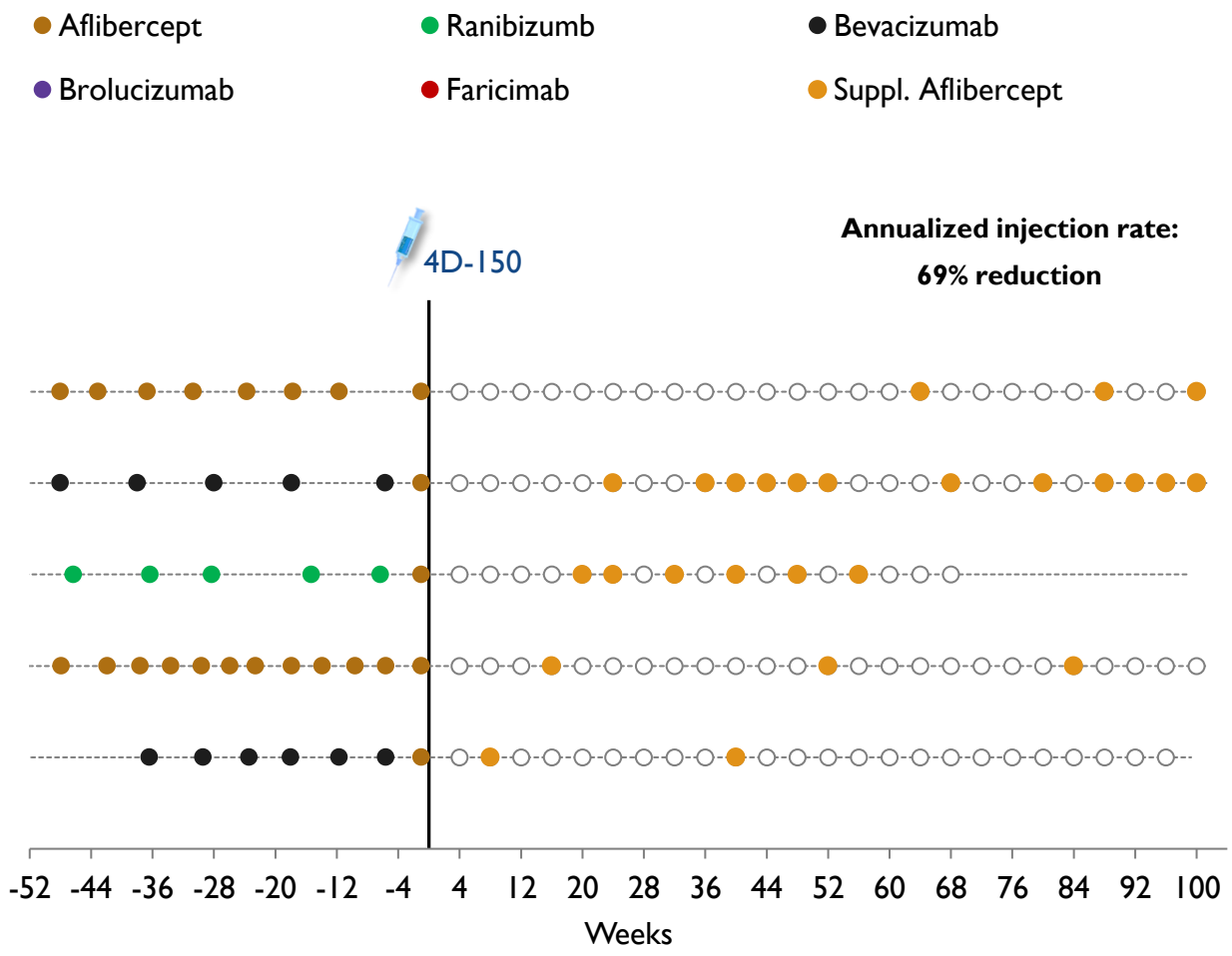
- 4 evaluable patients in 3E10 vg/eye (high dose & Phase 3 dose)
- 3 patients remain injection-free for 2-2.5 years & evaluable for 4D-150 expression; all available data shown through last aqueous humor collection timepoint (24 months)
  - 1 patient injection-free until ~9 months; AH alfibercept below level of quantitation



Data cutoff, September 3, 2024.

Baseline Characteristics & Treatment Burden Reduction: Phase 1 (6E9 vg/eye)

Characteristic	4D-150 6E9 vg/eye N=5
Mean ±SD age, years	76 ± 11.0 63–91
Mean ±SD BCVA, ETDRS letters	75 ± 8.9 62–84
Mean ±SD central subfield thickness, µm	402 ± 190.2 281–734
Mean ±SD time since diagnosis, years	4.7 ± 3.2 1.3–8.4
Mean prior *annualized* injection rate*	8.8
Mean ±SD *number* injections, prior 12 months*	8.4 ± 2.6 7–13



Data cutoff, September 3, 2024. *Includes Day -7 AFLB injection. BCVA, best corrected visual acuity; VEGF, vascular endothelial growth factor.

4DMT

Appendix 2:

PRISM

Phase 2b Interim Data

Follow-up: Through up to 52 weeks

4D-150 3E10 vg/eye, 1E10 vg/eye (N=45)

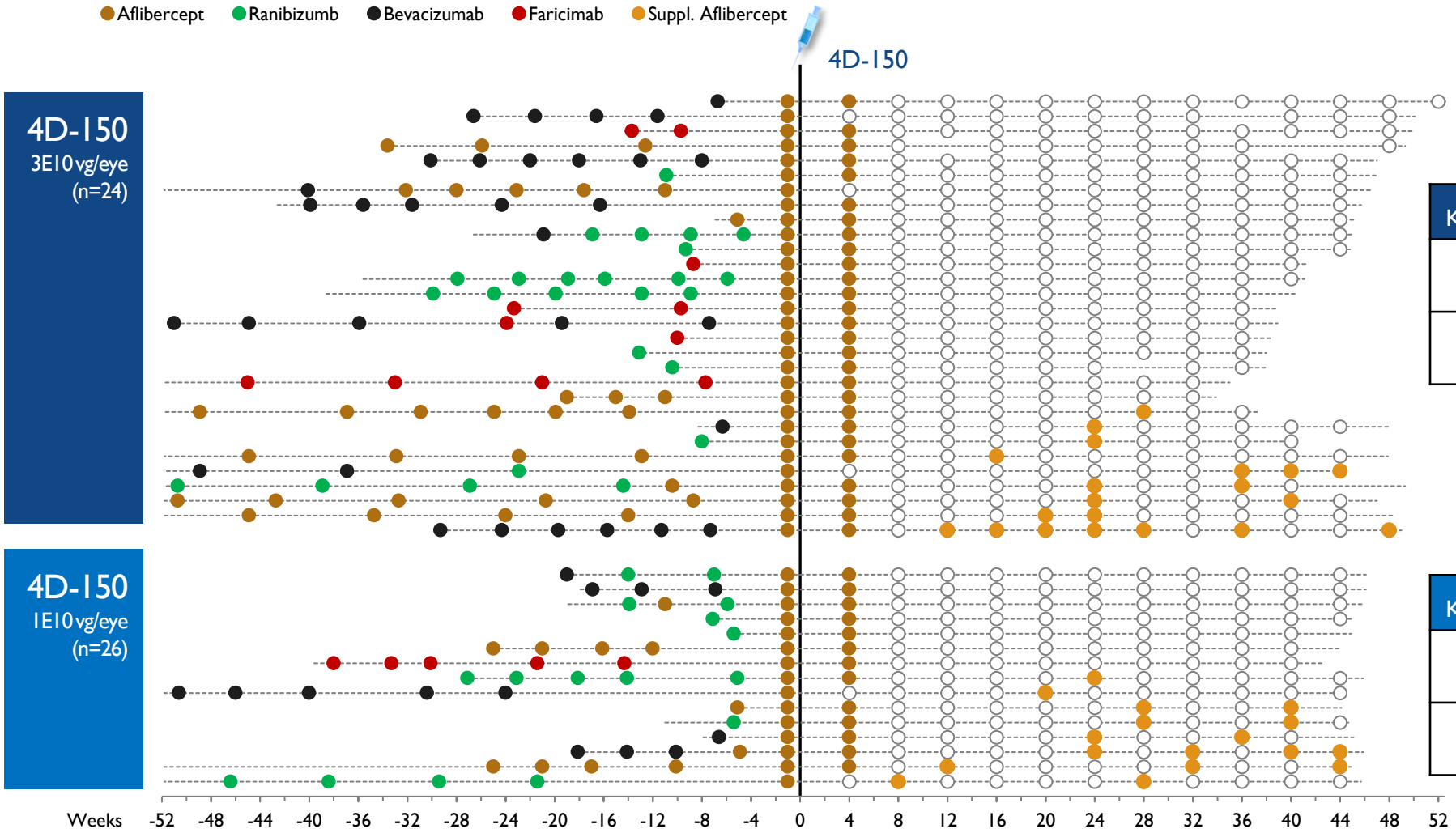
Data Cutoff Date, September 3, 2024

Baseline Characteristics: Phase 2b (Population Extension)

	3E10 vg/eye (N=30)	1E10 vg/eye (N=15)	Total (N=45)
Mean ±SD age, years	77 ± 7.7 62–92	78 ±8.6 *63–90*	77 ± 7.9 62–92
Female, n (%)	20 (67)	6 (40)	26 (58)
Race, n (%) White Asian	 30 (100) 0	 14 (93) 1 (7)	 44 (98) 1 (2)
Mean ±SD BCVA, ETDRS letters	71 ± 9.9 45–83	73 ±8.8 *51–80*	72 ± 9.5 45–83
Mean ±SD central subfield thickness, µm	336 ± 135.0 188–702	314 ±70.8 *225–441*	329 ± 117.1 188–702
Mean ±SD time since diagnosis, years	1.8 ± 3.4 0.1–13.9	0.7 ±0.9 *0.1–3.0*	1.4 ± 2.9 0.1–13.9
Mean prior *annualized* injection rate*	8.3	10.7	9.0
Mean ±SD *number* injections, prior 12 months*	4.4 ± 2.0 2–7	4.3 ±2.1 *2–9*	4.4 ± 2.0 2–9

*Includes Day -7 AFLB injection. BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; SD, standard deviation; VEGF, vascular endothelial growth factor.

Phase 2b:
Robust Reduction in Anti-VEGF Injection Treatment Burden in Both Doses

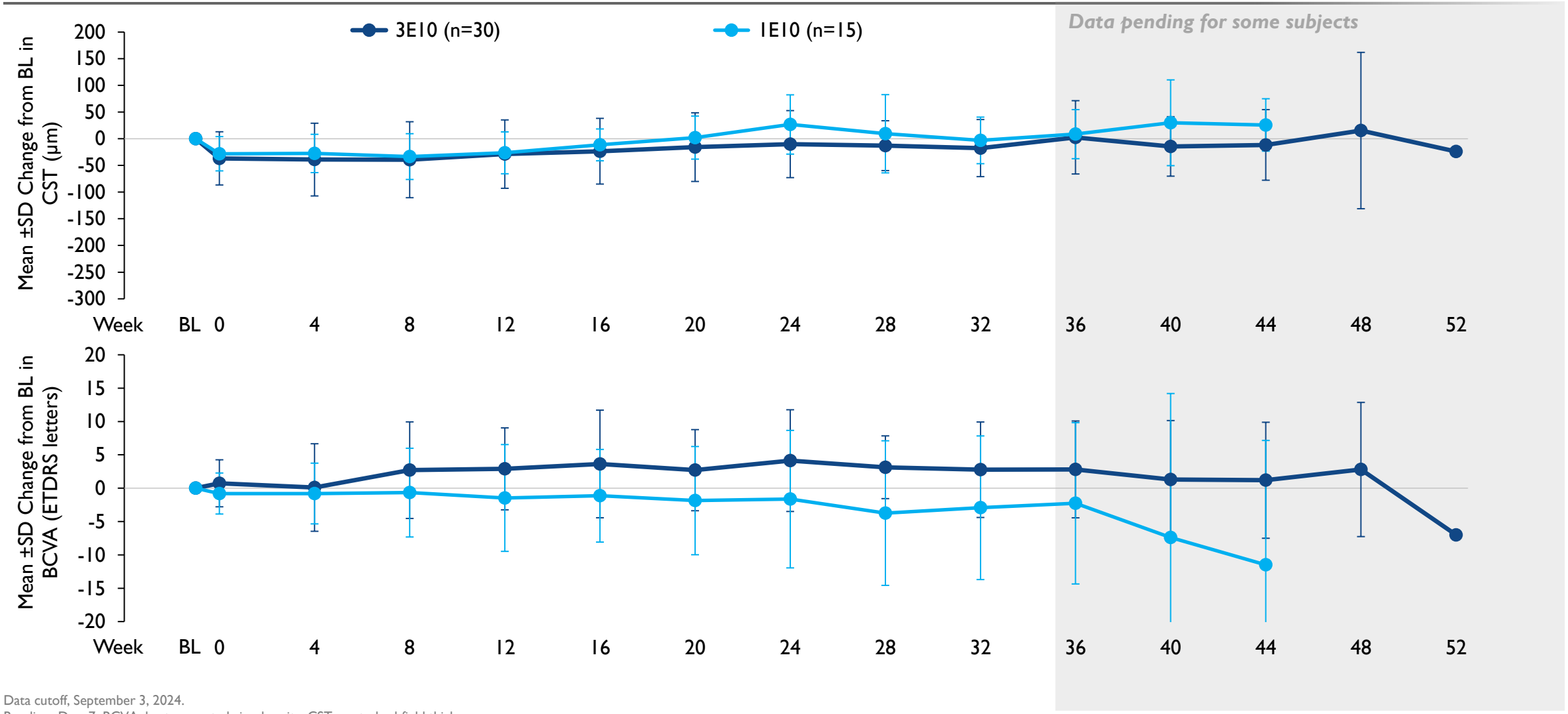


KM Estimate	W24	W36	W52
Injection Free	87%	70%	70%
0–1 Injections	97%	90%	80%

KM Estimate	W24	W36	W52
Injection Free	73%	47%	47%
0–1 Injections	100%	80%	60%

Data cutoff, September 3, 2024.

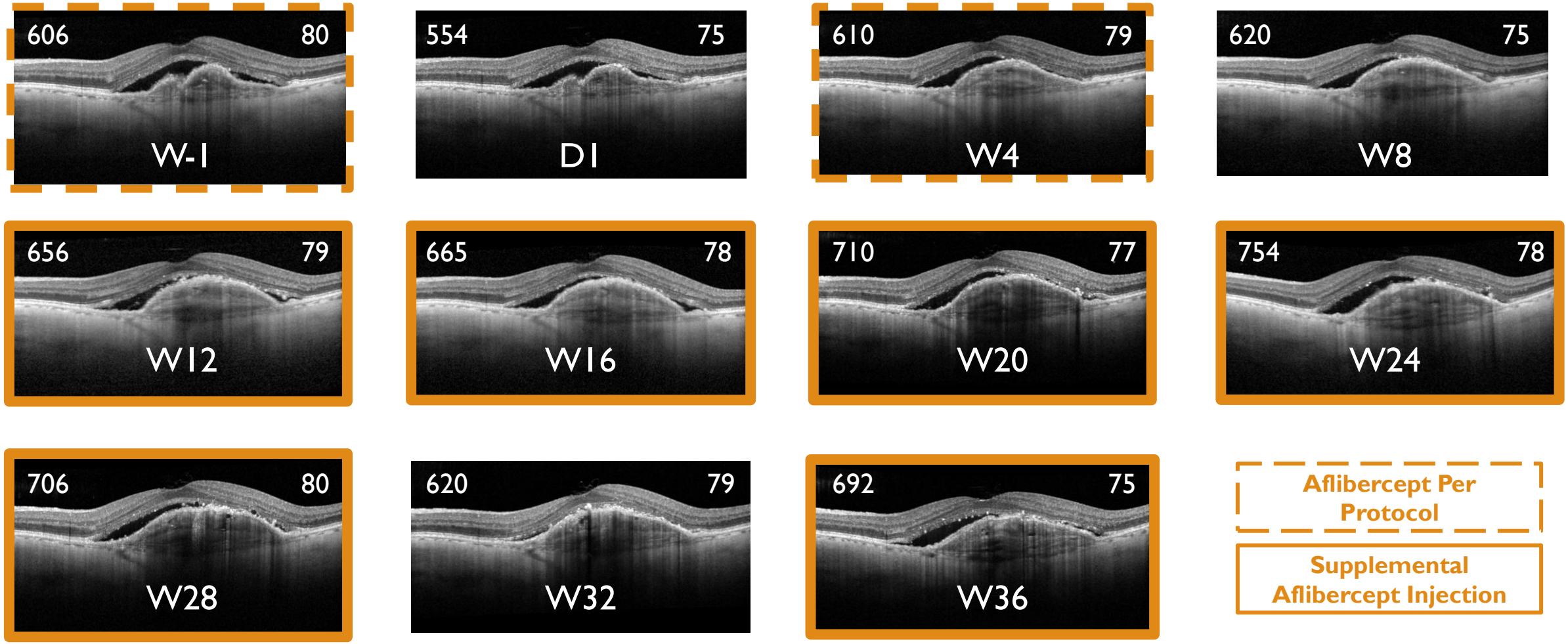
Phase 2b: Visual Acuity and Anatomic Outcomes Stable



Data cutoff, September 3, 2024.
Baseline=Day -7. BCVA, best corrected visual acuity, CST, central subfield thickness.

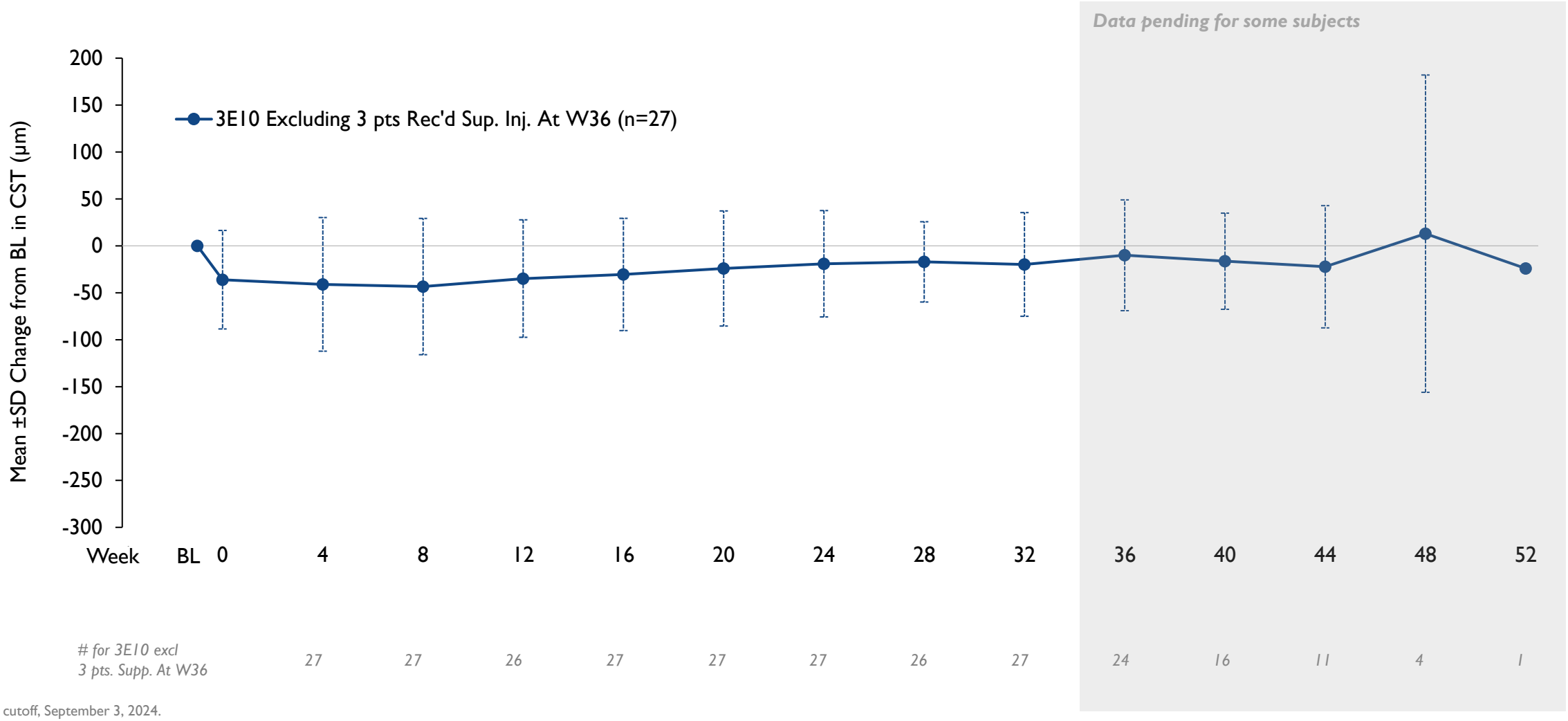
Patient Who Received Supplemental Injection at Week 36

Minimal Response Despite 8 Aflibercept Injections Over 9 Months



Data cutoff, September 3, 2024.

Phase 2b: 4D-150 3E10 vg/eye Sustained Anatomic Control With Fewer Fluctuations in 24 of 27 Patients Through 36 Weeks



Data cutoff, September 3, 2024.
Baseline=Day -7. CST, central subfield thickness.